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LUMBAR SYMPATHECTOMY FOR ARTERIOSCLEROSIS OF THE LOWER EXTREMITIES*

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BOSTON

MEDICAL therapy has been disappointing in the painful and disabling effects of arteriosclerosis of the lower extremities. In the past fifteen years an increasing number of patients have been subjected to the operation of lumbar sympathectomy in an effort to improve results. The present report, which is an analysis of 100 patients with arteriosclerosis subjected to this operation, is presented to add to the evidence, already in the literature,[1-10] of the value of the procedure in this disease.

It is hoped that this analysis will aid in answering certain questions that arise when this operative treatment is proposed for the arteriosclerotic patient. Can one safely perform the operation? These patients are often elderly, and with arteriosclerotic impairment of function of vital organs, they seem to be poor candidates for surgery. Will the operation substantially improve the condition of the limb? If the immediate results are good, will the patient or the limb survive long enough to make the procedure worth while? Finally, can rules be formulated to predict which patient will do well, and which poorly?

TABLE 1. *Period of Follow-Up Study.*

PERIOD	NO. OF CASES
mo.	
0–6	22
6–12	11
12–18	27
18–24	13
24–30	6
30–36	5
36–42	10
42–108	6
Total	100

ANALYSIS OF MATERIAL

Patients

Of the 100 patients reported 27 were operated on at the Massachusetts Soldiers' Hospital, 45 at the Faulkner Hospital, and 28 at the Peter Bent Brigham Hospital. The cases studied were consecutive. The operations were performed within approximately three years in the first two groups and within about nine years in the last group. The patients were followed for an average of twenty months (Table 1).

Sixty-three patients had a single sympathectomy, 24 had two separate sympathectomies, and the remaining 13 underwent bilateral denervation at one operation — a total of 137 sympathectomies.

There were 79 male and 21 female patients. The ages varied from that of a thirty-four-year-old patient with juvenile diabetes to that of a man of eighty-two. Fifty patients were between the ages of fifty and sixty, and 33 were over sixty (Table 2).

TABLE 2. *Age of Patients.*

AGE	NO. OF CASES
yr.	
30–40	1
40–50	16
50–60	50
60–70	24
70–80	8
80+	1
Total	100

Diabetes was present in 27 patients. It was of less than ten years' duration in 16 and from ten to thirty years in 11. The insulin requirement was less than 15 units daily in 9 cases, 15 to 50 units in 14 and over 50 units in 4.

Visceral disease, especially of an arteriosclerotic nature, was frequent in the diabetic patients and only slightly less so in the nondiabetic patients. Counting only severe symptomatic disease one notes that 15 patients had had one or more attacks of coronary thrombosis; 18 others suffered from

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angina pectoris. Eight gave a history of heart failure. Five patients showed severe manifestations of cerebral arteriosclerosis. Although lesser degrees of renal disease were frequent, only 1 patient showed significant nephrosclerosis. Extreme hypertension was infrequent (Table 3).

The condition of the limbs indicated moderate or severe obliterative disease in all cases. The level of occlusion of the major arteries was checked almost routinely by oscillometry. In only 11 cases could a pedal pulse be detected. In the other patients, the popliteal was the lowest detectable pulse in 11, the femoral in 67, and the external iliac in 6. In 5 patients there was no palpable pulse below the level of the aorta.

TABLE 3. *Correlation between Blood Pressure and Result.*

BLOOD PRESSURE	GOOD RESULT NO. OF CASES	POOR RESULT NO. OF CASES
140/80 or below	37	2
140/80 to 180/100	42	2
Over 180/100	13	4

The probability of *impending necrosis* was judged from the local signs other than pulse loss. These included one or more of the following: rest pain, pallor on elevation of an unusual degree, rubor on dependency involving the entire foot or extending higher, and finally the presence of petechiae, localized spots of blue discoloration that did not disappear on elevation, or a diffuse slate-blue discoloration. Atrophy of the skin, including the toe pads, and atrophy of the muscles were noted in many cases.

TABLE 4. *Indications for Sympathectomy.*

INDICATION	NO. OF CASES	GOOD RESULT NO. OF CASES	POOR RESULT NO. OF CASES
Threatened or actual necrosis	70		
Precarious state of limb short of gangrene	41	36	5
Superficial necrosis toe, foot, or leg	19	19	
Gangrene of toe distal to base	6	6	
Deep necrosis proximal to base of toes	4	1	3
Claudication	30	27	3*

*These 3 patients failed to obtain improvement of claudication, but the nutrition of the foot was improved throughout the follow-up period.

Frank or imminent necrosis constituted the *indication for* operation in 70 patients (Table 4). In 30 patients claudication was the primary indication, without prominent signs of impending necrosis.

Early Results

The division between the early postoperative and the follow-up period is arbitrarily placed at two months. In the early period 8 patients had an unfavorable outcome, with 2 deaths and 6 thigh amputations (Table 5), leaving 92 patients who walked out of the hospital with varying degrees of improvement.

Study of the records of the patients with poor results allows a conclusion that 1 death and 4 amputations resulted from failure to halt a downhill course of the disease already established before operation, and in 3 patients the outcome was contributed to or caused by the operation.

The 92 patients classified as having good results included 1 who successfully underwent a transmetatarsal amputation and 6 who had a toe removed, immediately after the operation. These toes were gangrenous prior to sympathectomy, and the amputation wounds healed well. The favorable results were occasionally not noted until a few days after sympathectomy, and it was not uncommon to find improvement progressing over the subsequent weeks and months.

TABLE 5. *Early Poor Results of Sympathectomy.**

RESULT	NO. OF CASES
Patients made worse by operation:	
Deaths (from coronary thrombosis)	1
Thigh amputation attributable to operation	
1 by deep venous thrombosis, 1 unexplained	2
Failure to halt downhill course of disease in limb:	
Thigh amputation and death (cerebral and coronary thromboses)	1
Thigh amputations with recovery	4
Total	8

*Two per cent of patients did not leave the hospital; 6 per cent of limbs were lost.

Scrutiny of the results in relation to the preoperative problem is of interest. The poor results were all found in the 70 patients with threatened or actual necrosis (Table 4) and chiefly in those in whom the state of the limb was considered precarious. On the other hand, patients with localized areas of superficial necrosis, or those with gangrene limited to one toe, did well. Finally, the poorest results occurred in patients with deep necrosis proximal to the base of the toes, as might have been expected.

In the group of 30 patients in whom claudication was the outstanding problem, there were no deaths or amputations, but 3 failed to obtain any relief of the claudication. We have not classified these 3 cases as complete failures, since the nutrition of the feet was greatly improved. Many patients were disappointed that the symptom was still present, though the walking distance required to produce it was considerably increased. Several patients no longer noted claudication except on walking up a steep grade.

Postoperative complications, including those resulting in unfavorable outcome, may be divided into

general complications, those relating to the incision and those in the limbs (Table 6). The deaths and amputations considered here are those already mentioned in Table 5.

A note of explanation regarding the neuritic pain in the thigh is in order. This pain occurred to some degree in about half the patients, though it was severe only in 11, mostly all private patients. The pain began on about the tenth postoperative day, and was located deep in the anterior thigh. Occasionally, there was cutaneous hyperesthesia over some part of the anterior or medial aspect of the thigh, but it could be differentiated from genitofemoral hyperesthesia. In a few cases the knee jerk was diminished, and the quadriceps muscle underwent slight atrophy. The findings suggested some disorder of the lumbar plexus. The presence of this syndrome could not be correlated with unusual difficulty in the dissection or excessive retraction of the psoas muscle. The pain disappeared in all the patients, the disappearance requiring several days to several weeks.

TABLE 6. *Postoperative Complications.*

COMPLICATION	NO. OF CASES	OUTCOME
General:		
Pulmonary embolism	6	Recovery
Pneumonitis, urinary retention	1	Recovery
Atelectasis, right lower lobe	1	Recovery
Hemiplegia and coronary thrombosis	1	Death
Coronary thrombosis	1	Death
In the wound:		
Superficial wound abscess	1	Healing
In the limb:		
Deep thrombophlebitis of sound limb	1	Healing
Superficial necrosis of heel	2	Healing
Neuritic pain in thigh	11	Disappearance
Worsening of vascular status:		
By deep thrombophlebitis	1	Thigh amputation
By increase in gangrene	4	Thigh amputation
By undetermined mechanism	1	Thigh amputation
By propagation of thrombosis to femoral artery	1	Recovery

Late Results

The general status of the patients in the follow-up period was encouraging. Only 9 deaths occurred, at a time varying from two to thirty-six months, and were usually due to coronary thrombosis (Table 7). Six additional patients suffered nonfatal episodes of cardiac or cerebrovascular accident.

The condition of the limbs has been assessed in the 89 patients remaining alive to date. *Once the early period was passed there was only 1 further amputation on the operated side, and this was a year later.* The vascular status of the foot almost invariably continued to improve. The warmth and good color seen early usually increased progressively. Atrophy of the skin, subcutaneous tissue and muscles was often reversed, giving a plump, warm, pink foot. The condition of the foot continued to be good in several patients in whom the arteriosclerotic process had caused the loss of a previously palpable pulse, though in these cases claudication usually became more prominent. The disappearance of the previously palpable external iliac pulse was noted in 3 cases, the femoral in 2, and the popliteal in 1.

TABLE 7. *Deaths in Follow-Up Period.*

AGE AT OPERATION	PREVIOUS VISCERAL DISEASE	CAUSE OF DEATH	INTERVAL AFTER OPERATION
yr.			mo.
71	Hypertensive cardiovascular disease	Cardiac failure	2
58	Coronary thrombosis	Coronary thrombosis	5
53	None	Coronary thrombosis	12
70	Coronary thrombosis	Coronary thrombosis	12
65	None	Coronary thrombosis	17
66	Coronary thrombosis (cerebrovascular accident)	Coronary thrombosis	21
54	None	Gall-bladder operation	29
61	None	Unknown	32
57	Diabetes, nephritis and pellagra	Coronary thrombosis	36

Correlation of Results with General and Local Factors

The results were considered in relation to several factors, with the following conclusions:

No correlation could be made between *age* and result.

Details concerning the 27 diabetic patients (Table 8) indicated that *diabetes* exerts an unfavorable effect upon the outcome of the operation, since both deaths and a disproportionate number of the amputations occurred in this group.

There was some slight preponderance of *visceral disease* other than diabetes in the patients who did badly, but the group was too small to do more than suggest a slight correlation.

No effect could be found of the level of *blood pressure* upon the result in patients who had normal or moderately elevated levels, but a blood pressure over 180 systolic, 100 diastolic, as noted in 13 of our patients was associated with poor results in 4 cases (half the poor results as shown in Table 3).

TABLE 8. *Results in Diabetic Patients.*

	NO. OF CASES
Indication for sympathectomy:	
Threatened or actual necrosis	26
Intermittent claudication	1
Immediate outcome:	
Good result	22
Deaths	2
Thigh amputation	3
Late follow-up report:	
Patient died later	5

Two *local factors* appeared to exert an unfavorable effect upon the outcome. As already noted (Table 4), deep necrosis proximal to the toes existing prior to sympathectomy was followed by a bad result in 3 out of 4 cases. Contrariwise, the patients with superficial necrosis all did well, whereas a precarious state of the entire foot was followed by occasional unfavorable results. The second local factor associated with a poor result was the previous loss of the contralateral extremity. Of the 9 patients in this category, 4 had early amputation of the remaining limb. It should be noted that the sympathectomy was performed in 3 cases when the status of the remaining limb had deteriorated to a desperate point.

TABLE 9. *Calcification of Leg Arteries As Demonstrated by X-ray Examination in 52 Cases.*

CALCIFICATION	GOOD RESULT NO. OF CASES	POOR RESULT NO. OF CASES
None or minimal	23	4
Moderate	16	0
Marked	8	1

No correlation could be established with the *level of occlusion of the major arteries* except that no poor results were obtained in any of the 11 patients with some pedal pulsation.

The *degree of calcification* of the peripheral arteries as seen in the x-ray films of 52 cases (Table 9) appeared to have no bearing on the outcome.

Finally, no correlation could be made between the preoperative temperature *response to paravertebral or spinal anesthesia* and the outcome after sympathectomy, since none of the patients having bad results were tested. However, all 30 patients who were tested obtained good results, even though 9 showed a poor response (temperature rise of 1° to 4°F.), 3 showed no response, and 1 showed a fall.

DISCUSSION

Value of the Operation

It is apparent that the patients subjected to operation constituted a fair sample of patients with moderate and advanced effects of the disease, regarding age, general condition and state of extremities. One may assert that events proved that these patients were worth salvaging so far as their life expectancy and the further fate of their limbs were concerned. It seems further reasonable to conclude that the operation was significant in reversing the downhill course of their limbs, which would otherwise have gone on to pain, disability and certainly in many cases to amputation. The low mortality (2 per cent) in these patients emphasizes the relative safety of the operation.

Special mention must be made of the possibility that sympathectomy will actually harm a limb. This matter has been discussed by several authors, especially Atlas,[3] deTakats and others[6] and Freeman and others.[8] In the 2 patients subjected to thigh amputation presumably as a result of the operation, the mechanism in 1 was clearly that of venous thrombosis. In the other, as in several cases in the literature, the mechanism was undetermined.

At this time we have no other form of therapy that approaches sympathectomy in its immediate and long-range effectiveness. Attempts to obtain similar results by drugs or by local anesthesia have been disappointing. In our experience, sympathicolytic drugs such as Priscoline have little or no effect on the arteriosclerotic limb, and may even render the ischemia more profound by diverting blood to other parts whose vessels are more capable of dilatation. For emergency situations, such as arterial thrombosis, anticoagulants are of great importance, and with their use repeated or continuous local anesthetic methods must be used cautiously.

We must recognize, however, that sympathectomy is by no means a curative method, since it does not reopen the blocked major arteries. Its action is, of course, to increase *collateral* flow. As with all such methods, one cannot hope to restore the circulation to normal, since the flow in the aggregate of these small arteries will always be less than normal, according to the laws of hemodynamics.

CHOICE OF PATIENT

The decision to perform sympathectomy depends partly on the general condition of the patient, and partly on the state of the limb. We have so far established only two definite contraindications — namely, visceral disease of such severity that the patient might be expected to succumb to the operation and deep necrosis proximal to a toe.

Concerning the old or generally sick patient, it is apparent that the current problem in the limb must outweigh his general one. Practically, this means that claudication per se is not an indication in this group, but that actual or threatened necrosis short of the gangrene noted above is the real indication.

In a patient who is relatively young and robust, we have advised the operation whether the presenting problem has been claudication or actual or threatened necrosis. This point of view is based on the probability that without sympathectomy not only will claudication become worse in time but also necrosis will later occur.

Superficial necrosis, when located on the foot or leg, has yielded well to sympathectomy, but necrosis leading down to bone has healed but infrequently. It is uncertain whether or not sympa-

thectomy substantially improves the chances for healing of an amputation at toe or metatarsal level. We cannot agree with others that atrophy of the cutaneous structures is a contraindication. On the contrary, most of our patients showed this change and did well.

Preoperative prediction of the expected result of the sympathectomy is very difficult except that, as noted above, one cannot expect much in the presence of deep necrosis or gangrene. Of the other general or local factors that exert an unfavorable influence on the outcome, we may note the definite but not overwhelming effect of diabetes, and the slight effect of other visceral disease, and perhaps extreme hypertension. The unfavorable effect of previous loss of the contralateral extremity seems valid. It should be mentioned that, at least in diabetic patients, as many as 40 per cent of such surviving limbs not treated by sympathectomy ultimately come to amputation.[11, 12]

Preoperative testing of skin temperature of the foot, before and after paravertebral block or spinal anesthesia, is disappointing. One cannot expect much vasospasm in arteriosclerosis, and it may be recalled that it was precisely for this reason that sympathectomy was generally withheld from the arteriosclerotic patient for many years. There is now adequate evidence that a poor response to anesthesia is nevertheless usually followed by a good result after operation. In our experience a good result was also obtained even in cases showing no rise or a fall in temperature on performance of the preoperative test. This is contrary to the opinion generally held. We conclude that a good temperature response to anesthesia predicts a good response to operation, but that failure to respond to the test does not necessarily foretell a poor result from the operation.

Management

Certain details that have been found useful in the management of these cases may be noted briefly. An extraperitoneal approach is probably easier for both patient and surgeon than a transperitoneal operation. Splitting the muscles rather than cutting across them gives a stronger closure, with less likelihood of hernia.

A foot in precarious condition should be carefully protected from pressure, elevation above heart level or the application of heat. The condition of the foot may be worsened for a few hours immediately after the operation. During this time irreparable damage may be done, perhaps by thrombosis of terminal vessels. Our procedure in these cases is to elevate the head of the bed to place the heart above toe level, and to give heparin within one or two hours. Some sort of anticoagulant therapy should be strongly considered in all the patients, because of their great tendency to arterial and venous thrombosis. In cases not immediately critical, heparin may be started within several hours, or Dicumarol may be given on the patient's return to bed.

Summary and Conclusions

An analysis of 100 patients with symptomatic arteriosclerosis of the lower extremities subjected to lumbar sympathectomy is presented. The cases were representative of the problem in age, the presence of visceral disease and the severity of the process in the limbs. Twenty-seven were diabetic patients.

There were 2 hospital deaths, and 6 early thigh amputations. Ninety-two patients left the hospital improved.

The patients were followed for varying periods up to three years, and a few up to nine. The average follow-up period was twenty months. In this time 9 more patients died. The 89 patients now living have done well. The sympathectomized foot after unilateral operation has been almost invariably better than its unoperated fellow. There has been only 1 further amputation of the problem limb.

Patients with necrosis down to bone proximal to the toes did so badly as to suggest that this finding constitutes the only definite contraindication to the operation.

A moderately unfavorable influence was exerted by the presence of diabetes and a lesser influence by other visceral disease, and perhaps also by extreme hypertension. The previous loss of the contralateral limb was an unfavorable factor.

No correlation could be made between the following factors and the outcome: age, sex, the level of blood pressure between low limits and moderate hypertension, level of occlusion of the major arteries, or the degree of calcification of the arteries apparent in the x-ray film. Although a good temperature response to a paravertebral or spinal anesthesia predicts a good result from operation, failure to respond to the test bears little or no relation to the outcome.

The operation should be more widely applied to the arteriosclerotic patient, for he does very well, and both the patient as a whole, and the limb, are worth salvaging.

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THE PROBLEM OF THE MEDICAL LABORATORY TECHNOLOGIST*

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THE serious shortage of *properly qualified* medical technologists has been reflected again and again in the frequently inaccurate results of test specimens sent by the Voluntary Laboratory Approval Authority of the Massachusetts Department of Public Health to participating laboratories during the past ten years. It has become a matter of such grave concern that a group of laboratory directors, technologists and educators induced the Central Health Council to appoint a study committee, of which the writer is chairman, to seek means of alleviating this distressing situation. A subcommittee has gladly acted in an advisory capacity in the establishment of at least two new schools for medical technologists. Any academic educators interested in the establishment of other such schools or courses are invited to communicate with Dr. Donald A. Nickerson, pathologist at the Salem Hospital.

It was believed by the entire group that the first attack should be broadly educational; to this end the following three papers are presented by members of the committee as a guide and a challenge to the solution of this important problem.

*These remarks and the following three papers were presented as a symposium on the subject "What About Medical Laboratory Technologists?" at the annual meeting of the Massachusetts Medical Society, Boston, May 17, 1950, and were presented in part at a meeting of the Massachusetts Hospital Association, Boston, January 26, 1951.

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EDUCATIONAL REQUIREMENTS OF MEDICAL TECHNOLOGIST

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THE training of the medical technologist is extremely varied, owing in large measure to the rapid growth of the hospital laboratory over the last forty years. Qualifications were not seriously considered when a few simple routine tests were performed. However, the importance of the laboratory in diagnosis has been established, and with the ever-increasing number and complexity of examinations, it becomes quite clear that only well trained, intellectually honest personnel should be employed. The American Medical Association has suggested certain minimum standards, listed below, but it remains for the profession itself to attract those who might properly qualify. The experience of most college educators is that students will not enter this field when industrial and research laboratories offer better working conditions and a much higher financial return.

The education of the medical technologist falls into two phases: academic and professional. The professional training is given in the hospital laboratory. It should be well organized and under the direction of a competent clinical pathologist. The American Medical Association has set up such training programs under the term of "approved school of medical technology." Those who wish to become medical technologists, as well as members of the medical profession, should thoroughly understand the purposes of such a school. An "approved school" is a *professional training school* conducted in a manner acceptable to and approved by the Council on Medical Education and Hospitals of the American Medical Association with the co-operation of the American Society of Clinical Pathologists. On satisfactory completion of the training program, a trainee may take an examination offered by the Board of Registry of the American Society of Clinical Pathologists and become a Registered Technician. To enter an "approved school," one must be able to satisfy certain requirements: essentially *two years* of college work, including specified courses in biology and chemistry. The intent of the program is to offer a practical approach to the problems encountered in the clinical laboratory, and to better the standards of the technologists. Such a school constitutes the hoped-for *minimum* professional training of the technologist, and is the *only school*

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of this type sponsored by the American Medical Association.

However, the extra year of training in an approved school, in general without pay and at the student's own expense, is the chief stumbling block to encouraging the college graduate to enter this field. In the Department of Biology at Simmons College this year, students were offered, on the average, a choice of any one of three positions, all starting in at reasonable pay for an inexperienced college graduate. One unusual offer came from a laboratory (not clinical) willing to train the person chosen at its own expense, and to pay her a beginning salary of $2900 per year, *during training.* Such offers leave the educator with few arguments in favor of medical technology.

No uniformity appears to exist in the academic training of technologists. Thus, there is great variation in the qualifications of both those who

TABLE 1. *Approved Schools for Medical Technologists in Massachusetts.**

LOCATION	MAXIMUM ENROLLMENT
Beverly:	
Beverly Hospital	2
Boston:	
Faulkner Hospital†	2
Massachusetts Memorial Hospitals†	12
New England Deaconess Hospital	4
New England Hospital for Women and Children†	5
Fall River:	
Truesdale Hospital	4
Fitchburg:	
Burbank Hospital	2
Holyoke:	
Holyoke Hospital†	6
Lawrence:	
Lawrence General Hospital	3
New Bedford:	
St. Luke's Hospital	2
Newton:	
Newton-Wellesley Hospital	2
Pittsfield:	
St. Luke's Hospital	2
Quincy:	
Quincy City Hospital	6
Salem:	
Salem Hospital	4
Springfield:	
Mercy Hospital	6
Taunton:	
Taunton State Hospital	2
Tewksbury:	
Tewksbury State Hospital and Infirmary	2
Worcester:	
Worcester City Hospital	6
Worcester State Hospital	4

*Based on Hospital Service. Approved schools for medical technologists (*J. A. M. A.* 143:102-108, 1950).
†Affiliated with a college.

are active in the field and those who may be available for employment. Candidates appear to be drawn from the following educational levels: high schools; private vocational schools; training in military services; junior colleges; senior colleges; and graduate colleges. It cannot be said that the first three groups offer much in the way of theoretical training. Personnel from these groups should perform only routine tests, and then under the supervision of a qualified technologist. One difficulty appears to be that personnel with this restricted training who are employed to do specific kinds of work are at present performing tests for which they have no background. This may result in very grave errors. The private vocational schools are those licensed by the State Board of Education. There are three such schools in Massachusetts, with an enrollment of approximately 150 students. The extent of training (academic and professional) is varied, and it is difficult to obtain clinical experience for students. However, these schools offer a greater supply of technicians than other preparatory institutions, but like high schools and military services do not offer sufficient theory.

The last three groups — junior colleges, senior colleges and graduate colleges — may be considered as a unit. Obviously, the more years spent in academic training, the greater the theoretical background, and the better the understanding of clinical tests and, in general, the development of a more responsible person. All these groups offer sufficient courses in chemistry, biology and mathematics to fulfill the requirements of the American Society of Clinical Pathologists, but generally the training is not directed specifically with the medical technologist in mind. No connection exists between any of the Massachusetts junior colleges and an approved hospital training school. The nearest junior college affiliated with a Massachusetts hospital is Colby Junior College at New London, New Hampshire, where a program has been set up specifically designed for the purpose. Two senior colleges, Simmons College and the University of Massachusetts, have programs in affiliation with approved training schools. The Simmons program, in affiliation with the Faulkner and the Massachusetts Memorial training schools, is a graduate program, with a prerequisite of a bachelor's degree, and such courses as have been outlined by the American Society of Clinical Pathologists during undergraduate study. This program is never filled to capacity, despite excellent publicity given it by the college. Many Massachusetts senior colleges have recently shown interest in such programs, but unfortunately do not believe that the time has yet arrived — at least from their point of view — to set up special programs for the preparation of medical technologists.

Massachusetts has 19 approved (hospital) schools with a capacity (maximum) for training 76 students (Table 1). Four of these approved schools are affiliated with colleges.

Certain procedures seem desirable if more and better trained technologists are to be available:

Informing high-school and other noncollege students of the type of training required for medical technologists.

Encouragement of junior and senior colleges in the establishment of specific training programs for medical technology.

Subsidization (at least in part) of the student during training at an approved school.

TRAINING OF THE MEDICAL TECHNOLOGIST

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IN 1928 the American Society of Clinical Pathologists established the registry examination. Until 1933 any medical technologist in the field was eligible for registration. Until 1938 one year of college with certain minimal sciences was required. Until 1948 two years of college study including courses in certain sciences constituted the eligibility requirement for examination. In 1948 an additional year in an approved school of medical technologists — that is, one year of rotating laboratory internship — was added to these standards. A third year of college is now forecast in a United States Department of Labor report on employment outlook. The approved schools of medical technologists are under the Council of Medical Education and Hospitals of the American Medical Association, and they are the only schools approved by the Association. The registry has come to be recognized as the only authoritative qualifying body for this field by such medical organizations as the American Medical Association, the American College of Surgeons, the American Hospital Association and the Catholic Hospital Association and by pathologists, physicians and hospital superintendents. The standards described above are minimum, and show the progress, over a twenty-year period, in setting up as a goal the best standards the field has yet offered to help the physician make an accurate diagnosis for his patient.

The unfortunate truth is, however, that the majority of medical technologists do not meet even these minimum requirements. Of 918 hospital technologists in this state, only 135 are registered. Of 187 questionnaires returned in a recent survey of Massachusetts, 40 per cent had college degrees, and 75 per cent of these were registered. Of the remaining 60 per cent, many regret their own poor training in private trade schools and the fact that they were not properly informed about the registry requirements of the American Society of Clinical Pathologists before entering the field. Laboratory procedures performed by unqualified personnel have been known to result in grave errors in diagnosis.

This year the medical technologists have attempted to do something about the situation. The Massachusetts Association of Medical Technologists, Incorporated, originally chartered in Worcester in 1945, has been expanded through the efforts of the American Society of Medical Technologists and is now a statewide organization of medical technologists registered with the American Society of Clinical Pathologists. Successful scientific meetings have been held in Worcester (April, 1949), Pittsfield (October, 1949) and Boston (May, 1950). Locally, there have been affiliated chapters, whose voting members and officers include both registered, M.T. (ASCP), and nonregistered technologists, and which are actively supporting the American Society of Medical Technologists, sponsored by the American Medical Association.

This national group is composed of technologists registered with the American Society of Clinical Pathologists. In a recent statistical survey by this group's Standards and Studies Committee, the numbers of personnel with college degrees according to 3885 questionnaires answered, were as follows: A.B., 1420; S.B., 1508; M.A., 149; M.S., 195, M.D., 7; Ph.D., 21; and D.D.S., 1. In June, 1949, the United States Department of Labor, quoting statistics from the same report, stated that the American Society of Medical Technologists was the national majority group in the field.

The official organ is the *American Journal of Medical Technology*, and during the year, each member receives good scientific papers, some presented at the previous national convention, as well as notes of interest, announcements, recommended textbooks and discussion of new problems coming up in the society, such as recent ones on UNESCO. The American Society of Medical Technologists, whose members may also practice in Hawaii, Puerto Rico, Alaska and Canada, is now being recognized internationally.

Although the Veterans Administration has received literature from the Society, inadequately trained veterans continue to apply for jobs. The tragedy here has been that all too often much of the so-called veterans' bill of rights has been misused. In each case the recommendation has been to go back to college with the suggestion that in this area Northeastern University has a two-year curriculum that may lead to a four-year program and a degree, as has the University of Massachusetts.

In mentioning the American Society of Clinical Pathologists registry examination, it might be well to discuss other examinations, which could be a possible source of confusion. There is another national group, the American Medical Technologists by name, organized in New Jersey and sponsored by the American College of Medical Technologists. (This constitutes recognition by themselves, since the college is set up by their own members.) Therefore, the American Medical Technologists always exert pressure for a state licensure, since they lack

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recognition by the American Medical Association. The differences between the two societies are few but important. Inadequate eligibility requirements are asked by the American Medical Technologists (two years of college in addition to one year of rotating laboratory internship are required by the American Society of Medical Technologists). The examination of the New Jersey group is given in the presence of a physician. However, a three-hour proctored and difficult examination is given at an American Medical Association laboratory school by the American Society of Clinical Pathologists Registry. Last but most important, the American Medical Technologists are *not* recognized by the American Medical Association. The American Society of Medical Technologists is the only one recognized by the American Medical Association.

Besides stimulating the medical technologists of the state to better themselves, by taking voluntary advantage of educational opportunities, the Massachusetts Association of Medical Technologists has set up a registry exchange enabling members to find employment suitable to their abilities. At present there are no medical technologists, registered with the American Society of Clinical Pathologists, available. Although only started last October, the exchange has heard from all the New England States and Canada. The projected demand for American Society of Clinical Pathologists personnel, of which there are nationally some 14,000, is 45,000 by 1960. If Massachusetts now had 900 such registered personnel, the need would be about 2700 by 1960. It is hoped that the shortage of pathologists and technologists will be overcome to help many over-all serious laboratory problems, which are city, state and nation wide.

SUMMARY

A brief history of the American Medical Association educational standards for medical technologists is given, with statistics to show that the majority of technologists in Massachusetts do not meet these minimum standards. The American Society of Medical Technologists is acutely aware of the situation and has tried this year to help both registered and nonregistered persons through education.

In contrast to the American *Society* of Medical Technologists, which is recognized by the American Medical Association (note confusing similarity of names), registration with the *American Medical Technologists* is *not recognized* by the Association.

The help of all Massachusetts Medical Society members is needed to correct a serious situation.

PROBLEMS IN THE MAINTENANCE OF ADEQUATE LABORATORY STAFFS

DONALD A. NICKERSON, M.D.*

BOSTON

THE changing pattern of medical care in recent years has resulted in a tremendous expansion of the activities of the clinical laboratory. In my personal experience, which I know is not unique, the past decade has seen a 400-per-cent increase in the volume of laboratory examinations done on patients in the hospital. This has been accompanied by a comparable increase in the number of technicians employed. Ideally, these technicians would have had a minimum of two years of college training, preferably a degree, would have the hospital internship, and would have been certified by the American Society of Medical Technologists under the sponsorship of the American Society of Clinical Pathologists. However, when one stops to consider the fact that facilities for training of technicians over that decade have remained almost stationary until the past two years, it is obvious that it has been impossible to meet the demand on the labor market. Therefore, many directors of laboratories have had to employ technicians with improper training. Many of them have had no college background, and no satisfactory hospital experience. When the fact that there is a 47 per cent annual turnover for better salaries and a 25 per cent turnover because of marriage is superimposed upon this demand for technicians, one can readily understand the problems encountered in obtaining the type of technician one would like to have in the laboratory.

To illustrate the need for better trained technologists one can examine the results of surveys of the work performed in hospital laboratories. One example is the report of the survey by Dr. W. P. Belk, who submitted solutions for analysis to a number of hospital laboratories in Pennsylvania. Figure 1 presents the results of such a procedure as blood sugar determination. Standards of 60 and 375 mg. per 100 cc. were sent to 92 participating hospitals. The results showed that the standard of 60 mg. per 100 cc. was reported in a range varying from 30 to 571 mg. per 100 cc. The 375 mg. per 100 cc. was reported in a range from 60 to 700 mg. per 100 cc. Only 50 per cent of the hospitals reporting were within an allowable range of error. Yet it is obvious that the blood sugar determination, which is important and may result in erro-

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neous diagnosis or therapy, demands dependable technicians using dependable technics.

What are some of the reasons for such results? An outstanding one is that the workload is so great that careful, accurate technics cannot be carried out. It is extremely difficult to assess an average workload on technicians on a state or national basis. However, it is my opinion that technicians working in general-hospital laboratories cannot adequately perform more than 10,000 procedures per year per technician. Another way of putting it is

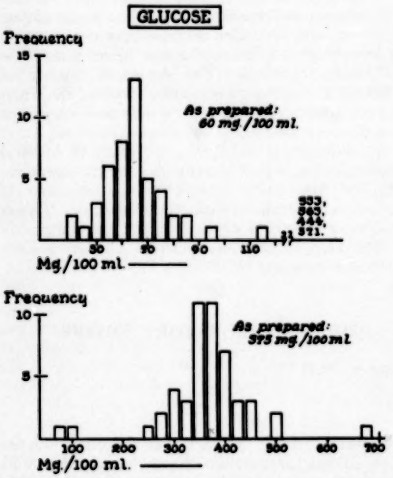

FIGURE 1. *Frequency Distribution of Results Obtained in Different Laboratories on Samples of the Same Known Solution (Reproduced, with the Permission of the Publishers, from Belk, W. P., and Sunderman, F. W. Survey of Accuracy of Chemical Analyses in Clinical Laboratories.* Am. J. Clin. Path. **17**: *853-861, 1947.*)

that the laboratory should have 1 technician for each 25 to 30 adult beds.

A most important factor is inadequate equipment. It seems obvious that the clinical pathologist should have a departmental budget that will ensure proper equipment in good working condition to perform the type of laboratory procedures that are required in his hospital.

An equally important factor is inadequate training of technicians. For many years pathologists, hospital directors and physicians employing laboratory technicians in their offices have not seen fit to differentiate technicians on the basis of their educational background, their training in hospital laboratories or their certification by the American Society of Clinical Pathologists. Physicians should acquaint themselves with the fact that there are organized groups interested in this problem and should become familiar with the American Society of Clinical Pathologists and the American Society of Medical Technologists.

Another great problem in the maintenance of an adequate laboratory staff is the matter of adequate salary. Here, again, technologists have not been properly differentiated on the basis of their training, experience and certification. It has been extremely discouraging for well trained technicians to work side by side with those having minimal qualifications and yet receiving the same salary. It is also true that, in general, salaries of laboratory technicians have been kept at a relatively low level, and this has been a real deterrent to girls with a college degree, who can see no reason for giving a year as an intern in a hospital laboratory when they can enter private industry at a considerably higher starting salary than they can command after their apprenticeship in a hospital laboratory. The experience of placement bureaus in some of the larger universities can document these statements.

A recent nation-wide survey by the American Society of Clinical Pathologists has shown that 10 per cent of all technicians change their positions for a 10 per cent increase in salary. It seems unreasonable that hospital pathologists and directors of hospitals cannot see fit to compensate qualified technologists properly, when the productivity, and even more important, the performance of satisfactory work greatly outweigh the small amount of increased expense.

Another factor is inadequate supervision of the technologists. This problem is, of course, greater in the smaller hospitals, particularly institutions that are a considerable distance from the larger cities. The number of clinical pathologists available is still small, and it is customary for many small hospitals, especially those under 100 beds, to have only part-time coverage by a pathologist; the amount of supervision of the laboratory is naturally minimal and often dangerously low. Attempts should be made to obtain the services of a pathologist on such a basis as will give adequate coverage. Perhaps the utilization of extension service tying the smaller hospital in with the larger hospital can satisfactorily meet this problem. Another arrangement would be to have several hospitals in reasonably close proximity engage a pathologist on a full-time basis and share his time among them as the need dictates. Concerted interest and effort on the part of medical staffs of these hospitals can do much to improve the situation from an ethical and financial standpoint, so that young pathologists will be attracted into these areas. If it is impossible to obtain the services of a pathologist, certainly a laboratory committee composed of interested members of the medical staff

should be appointed and should have the responsibility of supervising the laboratory to the best of their ability.

I have presented some of the problems. What can physicians do to improve the situation? First of all, the educational and hospital facilities for training people interested in this important field of medicine must be increased. There has been a distinct increase in the number of approved hospital laboratories during the last year, but there must be a marked acceleration within the next year or two. Even a 100 per cent increase in the number of approved schools in the next year will no more than meet the demand. Certainly, these young students cannot be expected to go to the other states for their training and return to Massachusetts looking for work. Opportunities for employment exist in every state. It is true that these college-trained people are expected to act as interns for a year, but one can make the situation more appealing by offering maintenance or a small stipend to the student with two years of college training and a minimal salary to the college graduate.

Secondly, I want to re-emphasize the point that physicians should acquaint themselves with the facilities for training technologists, and to be sure that those interested are properly directed.

Thirdly, physicians should show a real interest in the problems of the medical technologists. They should inquire of their own technicians whether or not they are registered and encourage those who are eligible to become registered. The salary schedule in the hospital or office provides an incentive for a properly trained technologist to become registered, and opportunities to take refresher courses should be offered to technicians.

Lastly, physicians should give active support to the pathologist to see that proper equipment is made available and that he has adequate numbers of properly paid technologists to share the workload. Those who practice in hospitals where a pathologist is not available should see if active steps cannot be instituted to arrange for a pathologist to be a member of the medical staff and to take over the active supervision of the laboratory and help face the problems that are so vital.

Summary

The steadily increasing volume of laboratory procedures is indicated, and the need for properly trained technologists is discussed. Factors resulting in the unsatisfactory performance of standard laboratory procedures are discussed, and steps to improve technologic personnel are suggested. It is suggested that co-operation by the clinician and hospital director would be invaluable assistance to the pathologist in a program to better laboratory facilities.

EFFECT OF CORTISONE IN SARCOIDOSIS*

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PHILADELPHIA

ALTHOUGH sarcoidosis is commonly considered a benign condition, it may occasionally be a serious illness, resulting in blindness, respiratory insufficiency or death. In a search for an effective therapeutic agent, many substances have been tried. Fowler's solution and x-ray therapy have been found ineffective.[1] More recently, benefit has been reported from the use of calciferol (vitamin D_3),[2] nitrogen mustard,[3] and urethane,[4] but in our experience neither these agents nor antibiotics have given consistent results.

Because it tends to involve many organs, sarcoidosis bears a clinical resemblance to certain of the disseminated collagen diseases. The hyperglobulinemia characteristic of sarcoidosis is also a feature of disseminated lupus erythematosus. Teilum[5] reported amyloid deposits in the reticuloendothelial cells of sarcoidosis identical with those observed in tissues of patients with amyloidosis and disseminated lupus and suggested that all three of these diseases represent an allergic hyperglobulinosis. Since sarcoidosis exhibits these similarities to diseases that have responded to the glucocorticoids, it seemed advisable to study patients with sarcoidosis to detect possible subclinical endocrine impairment, particularly of the pituitary and adrenal glands, and to determine the effect of Cortisone therapy in this disease. During the course of this study, Thorn and his co-workers[6] reported the use of ACTH in a case of sarcoidosis, without beneficial effect. Olson and his associates[7] described marked improvement of uveitis in 2 patients with suspected sarcoidosis treated by ACTH, but it was remarked in 1 case that no change was observed in the pulmonary involvement. Because of the disparity between these results and ours, this preliminary report seems indicated.

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Case Reports

Case 1. B. N., a 28-year-old Negress, born in Maryland, was admitted to the Woman's Medical College Hospital on April 1, 1950, with the chief complaint of a skin rash of 3½ years' duration. The patient was a college graduate employed as a high-school teacher. She appeared to be happily married and had one child. There was no past or family history of significant mental or physical illness. She had been in good health until the summer of 1946, when she had a spontaneous abortion, followed by 2 months of anorexia, malaise, lower abdominal pain and a 20-pound weight loss. Her physician administered a course of penicillin. In September, 2 days after the last injection, she noted a rash, described as "hives," on the extensor surfaces of her arms and over the lower legs. There were a few raised, rounded areas of lighter color than her skin, ranging in size from that of a pinhead to 1.3 cm. in diameter. The lesions developed rapidly within 4 to 7 days; they were not tender and did not itch. She thought that the rash represented a reaction to penicillin and did not return to her doctor for further treatment. The eruption remained unchanged until the fall of 1947, when the lesions increased in size and lesions first appeared on the face and lips. In December the right eye became red and painful. She consulted an ophthalmologist, who made a diagnosis of possible sarcoidosis and for 6 weeks treated her with streptomycin. The redness disappeared, but the corneal lesions remained. She subsequently received injections of bismuth, but despite treatment, corneal opacity increased.

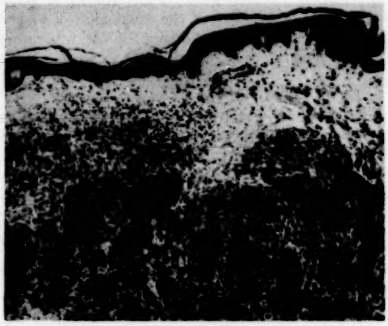

Figure 1. *Section of the Skin Biopsy before Treatment in Case 1, Showing Large Sarcoid Nodules within the Corium.*

In July, 1948, she was studied in a dermatology clinic. At this time a roentgenogram of the chest revealed hilar adenopathy and diffuse pulmonary infiltration. Biopsy of a waxy lesion on the left cheek showed sarcoidosis. The patient's condition remained stationary for the following 16 months. On November 1, 1949, she was referred to the Sarcoid Clinic at the Henry Phipps Institute of the University of Pennsylvania where BGG vaccination was performed. Tuberculin sensitivity failed to develop.[5] Liver biopsy showed a granuloma consistent with sarcoidosis. She was referred to to the Woman's Medical College Hospital for Cortisone therapy.

Physical examination disclosed a pleasant and co-operative patient who appeared to be under tension, presumably because of anxiety attendant upon hospitalization. She was afebrile and weighed 110 pounds. There was generalized lymphadenopathy involving the anterior and posterior cervical, epitrochlear, axillary and inguinal nodes. The largest nodes (epitrochlear) were about 1 cm. in diameter. The heart and lungs were normal; the blood pressure was 95/65. The liver edge was palpable three fingerbreadths below the costal margin. The spleen was barely palpable. The right eye showed marked ciliary injection at the lower limbus, a mature complicated cataract and posterior synechia; there was light perception only. The left eye was normal. Examination of the skin showed grouped nodular lesions up to 1 cm. in diameter on the chin, cheeks and forehead with some depigmentation of the surrounding skin, which was elevated by subcutaneous infiltrate. Arm and thigh lesions were scattered mainly over the extensor surfaces. There were scattered, brownish papules also on the inner nares and on the hard palate. The leg lesions were closely aggregated, flattened, brownish-red papules. Many of the leg lesions had necrotic centers that could be lifted out, leaving a small depression. The remainder of the physical examination was negative; no evidence of developmental or hormonal abnormality was found. Roentgenograms of the chest revealed hilar widening and scattered nodular infiltration showing no change from films of 1948 and 1949. Biopsies of the skin and cervical lymph nodes showed characteristic sarcoid lesions (Fig. 1).

Adrenal-function tests were made prior to treatment. The urinary 17-ketosteroid excretion of 5.9 mg. per 24 hours was below the values observed in this laboratory in normal women (7 to 17 mg. per 24 hours). The eosinophil count fell from 488 to 289 per cubic millimeter (41 per cent) in response to epinephrine. The blood ascorbic acid was 0.40 mg. per 100 cc., and the urinary excretion was 7.3 mg. per 24 hours. An increased tolerance was shown to orally administered glucose and the water-excretion index was 42. The basal metabolic rate was +16 per cent. Other significant laboratory findings included a sedimentation rate (Cutler method) of 32 mm. per hour, hematocrit of 40 and a white-cell count of 2800. The serum albumin was 2.0 gm. and serum globulin was 6.2 gm. per 100 cc. Liver-function studies were negative except for a +++ cephalin-flocculation test. Serum electrolytes were normal.

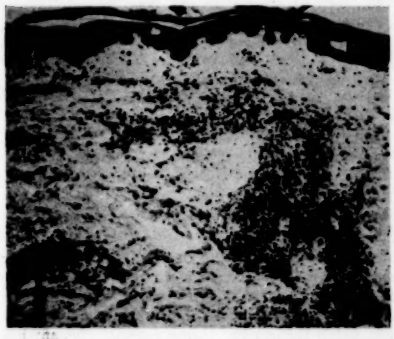

Figure 2. *Section of Skin Biopsy after Treatment in Case 1, Showing Chronic Inflammatory Reaction but No Sarcoid Lesions.*

A measured diet, standardized for intake of protein, carbohydrate, fat and ascorbic acid, was prescribed. On April 15, 1950, intramuscular administration of Cortisone in a dosage of 100 mg. twice daily was started. A total of 3 gm. was given over a period of 15 days. The weight, blood pressure, hematocrit, white-cell count and differential count, absolute eosinophil count and urinary 17-ketosteroids were determined daily. Within 48 hours of the start of treatment, the ciliary injection of the right eye was diminished, and flattening of the facial skin nodules was noted. At 72 hours, the ciliary injection of the right eye had disappeared, and there was more

marked flattening of the nodules of the face and extremities. On the 7th day of treatment the patient appeared elated over the change in her appearance. At this time some fullness of the face was also noted. On the 10th day, lip and palatal lesions had disappeared, with further retrogression of the skin lesions. No decrease was noted in the hepatosplenomegaly. On the 11th day a natural menstrual period occurred. Rounding of the facial contour became pronounced after the 13th day.

All control studies were repeated from the 13th to 15th days of treatment. Significant changes were an increase in weight of 8 pounds, slight increase in the sedimentation rate and a significant fall in the hematocrit. A polymorphonuclear leukocytosis and eosinopenia developed. There was increased excretion (8.2 mg. per 24 hours) of 17-ketosteroids, and the water-excretion index dropped to 20. The basal metabolic rate was −6 per cent. The eosinophil count fell from 67 to 11 per cubic millimeter in response to epinephrine. Serum sodium, potassium and protein concentrations were unchanged. There was an increase in the blood ascorbic acid level with a marked increase in urinary excretion of ascorbic acid. A roentgenogram revealed a definite decrease in the size of the hilar shadows and partial clearing of pulmonary infiltration. There had been a marked decrease in size of the cutaneous lesion and cervical lymph node, which had been selected as comparable to the lesions originally biopsied. Biopsies of these lesions disclosed a striking change (Fig. 2). There was no recognizable sarcoid structure. The appearance was largely that of chronic nonspecific inflammation.

At discharge on April 30 the patient was somewhat irritable and antagonistic, stating that she could not attend any more clinics. She was assured that arrangements would be made to see her when she had free time. In the hope of stimulating pituitary and adrenal function, which had been depressed by the Cortisone, epinephrine (1:1000 dilution), 0.2 cc. twice daily, was prescribed. Three days later the patient returned to the dispensary for removal of sutures from a biopsy site. Marked facial and leg edema was observed, and she appeared upset and agitated. She disappeared from the hospital as soon as her sutures had been removed and did not keep a scheduled appointment at the medical clinic. On the following day, word was received that she had collapsed at home after an epileptiform convulsion. A physician was called who reported that she was extremely agitated and definitely antagonistic toward everyone who had attended her at the hospital. She was finally persuaded to enter the Philadelphia General Hospital, where a diagnosis of paranoid schizophrenia, probably toxic in origin, was made. Edema had disappeared and all electrolyte studies were within normal limits. After five electroshock treatments she was discharged as improved, and when last seen by the attending psychiatrist, she seemed stable psychologically but refused to permit medical examination other than chest roentgenograms. Films on July 31 revealed that the improvement in the pulmonary infiltration had been maintained.

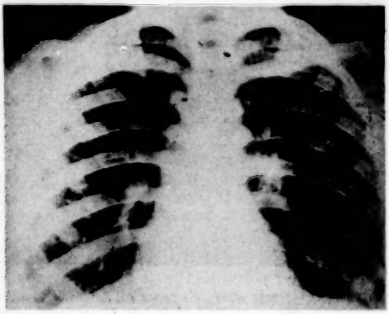

FIGURE 3. *Roentgenogram of the Chest before Treatment in Case 2, Showing Soft Miliary Infiltration throughout the Lung Fields and Moderate Enlargement of the Mediastinal and Hilar Lymph Nodes.*

CASE 2. M. J., a 20-year-old Negress, was admitted to the hospital on June 6, 1950, with the chief complaint of swollen glands. The family and past histories were not significant. The patient, an only child who lived at home with her mother, assisting in the operation of a hand laundry, had been in good health until March 1, when a stuffy nose, persistent, productive cough, headache and pain in the chest, arms and shoulders developed. She was treated symptomatically by her physician, with little relief. Later in March she noted bilateral swelling of the parotid and lacrimal glands. An x-ray film of the chest made in April revealed hilar widening and bilateral, diffuse nodular infiltrations. She was referred to the Sarcoid Clinic at the Henry Phipps Institute of the University of Pennsylvania. On June 2 the diagnosis of sarcoidosis was confirmed by biopsy of the left parotid gland, which revealed characteristic epithelioid cell tubercles without necrosis, and she was hospitalized for Cortisone therapy.

FIGURE 4. *Section of the Left Parotid Gland before Treatment in Case 2, Showing Large Sarcoid Nodules.*

On admission to the Woman's Medical College Hospital the patient offered no complaints except for the swelling of the eyelids and cheeks. Respiratory symptoms had subsided. A 30-pound weight loss had occurred between March and May, but appetite had returned and there had been no further weight loss. Examination revealed a markedly obese young woman, weighing 212 pounds. She was afebrile and not manifestly ill. There was obvious enlargement of the lacrimal glands, more marked on the left. Measurements with lids everted were as follows: right, 18 by 8 mm.; left, 14 by 5 mm. There was no ciliary injection, and funduscopic, slit-lamp and visual-field examinations were negative.

The parotid swellings were firm and granular to palpation, the right measuring 40 by 58 mm., and the left 50 by 78 mm. There were no skin lesions. Small posterior cervical, axillary and inguinal lymph nodes were palpable. The heart was normal; the blood pressure was 114/85. The lungs were clear and resonant throughout. The abdomen was obese; the liver and spleen were not palpable.

Roentgenogram of the lungs on admission revealed large hilar shadows, with soft miliary infiltrations throughout both lung fields (Fig. 3). Tuberculin and histoplasmin tests were

negative. Biopsy of the left parotid gland demonstrated characteristic sarcoid infiltration (Fig. 4). Significant laboratory findings included a sedimentation rate of 35 mm. per hour. Liver-function studies were negative. The serum globulin and albumin were normal. There was increased tolerance to orally administered glucose. The basal metabolic rate was −3 per cent. Urinary 17-ketosteroids were low, averaging 3.5 mg. per 24 hours (value normal women, 7 to 17 mg. per 24 hours). The water-excretion index was 9.1. The eosinophil count fell from 333 to 111 per cubic millimeter in response to epinephrine. The blood ascorbic acid was 0.56 mg. per 100 cc., and the urinary excretion 3.9 mg. per 24 hours.

A measured diet was given and standardized for intake of carbohydrate, fat, protein and ascorbic acid. Placebo in-

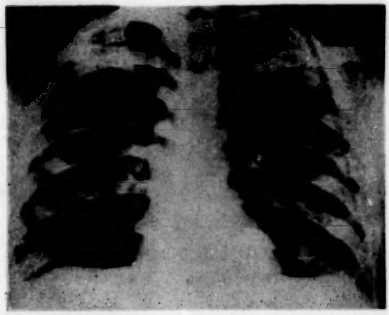

FIGURE 5. *Roentgenogram of the Chest after Treatment in Case 2, Showing Complete Clearing of the Pulmonary Infiltration. The chest appears normal except for a single enlarged lymph node in the upper right portion of the mediastinum.*

jections of cholesterol suspension were given twice daily for 6 days while baseline studies were performed, after which Cortisone was administered in a dosage of 100 mg. twice daily for 9 days. Injections of 100 mg. were given once daily for an additional 2 days, making a total dose of 2.0 gm. The following studies were performed daily: weight, blood pressure, complete blood count including hemoglobin, red-cell and white-cell counts, differential count, absolute eosinophil count, sedimentation rate, hematocrit and urinary 17-ketosteroids.

The lacrimal and parotid glands began to decrease in size within 48 hours. At the time of discharge from the hospital, the lacrimal glands were barely palpable; on eversion of the lids, the right measured 7 by 4 mm., and the left 10 by 5 mm. The parotid glands were no longer palpable. Roentgenogram of the chest at the end of treatment disclosed almost complete disappearance of the bilateral miliary type of infiltrations previously described (Fig. 5). An attempt at biopsy of the left parotid gland after treatment yielded lymphoid parotid tissue with recognizable sarcoid tubercles. Fibrosis and hyalinization were more marked than in the tissues obtained before treatment (Fig. 6).

Control studies were repeated at the end of Cortisone treatment. Significant changes included a slight fall in blood pressure and hematocrit. The excretion of urinary 17-ketosteroids increased to a normal level. The urinary excretion of ascorbic acid rose sharply, without change in the blood level. The water-excretion index fell to 6.0. The eosinophils fell from 56 to 22 per cubic millimeter in response to epinephrine. The oral glucose tolerance curve, basal metabolism, serum sodium, potassium and proteins and electrocardiogram showed no change. Psychiatric study after therapy revealed no manifestations attributable to the Cortisone treatment. When the patient was last seen on October 19 the improvement in lacrimal, parotid and pulmonary lesions was fully maintained.

DISCUSSION

The evaluation of therapy in sarcoidosis is extremely difficult because of the frequency of spontaneous remission. Marked improvement occurred spontaneously in almost half of 46 patients whom we have observed over a mean interval of five years. However, it is improbable that the marked and speedy regression observed in both patients in response to Cortisone was coincidental. The marked clinical amelioration was accompanied by striking changes in tissues obtained by biopsy after treatment. The greater improvement with smaller dosage observed in the patient in Case 2, whose disease was of shorter duration, suggests that Cortisone is most effective in the treatment of relatively acute lesions. The post-treatment psychosis suffered by the patient in Case 1 was severe and required electroshock therapy. The greater dose of Cortisone used may have been responsible, but it is probable that latent psychotic tendencies were present.

FIGURE 6. *Section of the Left Parotid Gland after Treatment in Case 2, again Showing Sarcoid Nodules but of Smaller Size.*

Investigation of the endocrinologic status of the patients was carried out before, during and after treatment. Impairment of adrenal function was suggested by certain laboratory findings: the abnormal eosinophil response to epinephrine in Case 1, the low water excretion index in Case 2 and the diminished 17-ketosteroid excretion in both patients. Evidence of functional adrenal impairment has not previously been reported in sarcoidosis, and further study is required to confirm these observations. The insufficiency may have been the result of

prolonged disease, but this seems unlikely since one patient had had symptoms of sarcoidosis for only three months. Adrenal insufficiency may account for the better therapeutic response observed with Cortisone than has been reported with ACTH. Further trial of both ACTH and Cortisone in sarcoidosis is in progress to determine more definitely their relative therapeutic value as well as to clarify the nature and extent of endocrinologic changes in this disease.

Summary

Endocrinologic study of 2 patients with severe and widespread sarcoidosis gave some evidence of impaired adrenal function. Use of Cortisone resulted in prompt and marked improvement in pulmonary, cutaneous, lacrimal, parotid and lymph-node lesions.

We are indebted to Drs. Carmen Thomas, Grace Nachod, Emilie Loeffler and Virginia Hartridge, of the Woman's Medical College Hospital, for their assistance.

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PROGRESS IN THE MEDICAL CARE OF THE VETERAN

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WITHIN the past four years the hospital program of the Veterans Administration has been thoroughly revised. Tremendous progress has been made toward a basic objective of providing the best medical care for veterans. This transformation, which is without parallel in the medical history of the country, has not been accomplished without certain misunderstandings and criticisms. This paper outlines the progress made and attempts to answer some of the criticisms that have been directed against the Veterans Administration.

First to be considered is the progress that has been made since the passage by the Seventy-Ninth Congress of Public Law 293, which removed physicians, dentists and nurses from the requirements of Civil Service. Previous deficiencies of the Veterans Administration medical program were well recognized by leaders of the medical profession in this country, and passage of this law gave them the freedom of action required to bring about necessary reforms. General Omar Bradley, who was appointed administrator of veterans' affairs, gave carte blanche to his chief medical director, Dr. Paul R. Hawley, to make whatever changes he believed necessary in a sweeping reorganization of the medical program.

An advisory group headed by Dr. Paul B. Magnuson, Dr. Elliott C. Cutler and others made specific recommendations, which were quickly implemented. One of the first of these was the hiring of capable medical personnel without reference to Civil Service rules and regulations. This permitted the Veterans Administration to attract to its staffs a large number of competent physicians and surgeons. Leading physicians in all the medical and surgical specialties were utilized on a part-time basis as consultants and attending physicians. Residency training programs were instituted in many of the hospitals under sponsorship of deans' committees from leading medical schools. The standards of practice and teaching in the Veterans Administration hospitals were raised to a par with those in leading university hospitals and private clinics. A description of the progress that has been made along these lines was recently published in this *Journal* and requires no further elaboration.[1]

In some of the chronic diseases, such as neuropsychiatric disorders, tuberculosis and medical rehabilitation, progress has been less spectacular but no less important. For example, in Veterans Administration neuropsychiatric hospitals the trend is to eliminate iron bars and grills and to substitute protection screens on windows and doors. The former gloomy atmosphere has been changed by the use of light-colored paint on woodwork and pastel shades on walls. Bright-colored draperies and chair covers in dining halls add much to the cheery atmosphere. Table linens are used in all dining halls, and all except a few highly disturbed patients are authorized to use the full complement of knives, forks and spoons rather than being limited as in many neuropsychiatric institutions, both past and present. Deep insulin-shock therapy, electric-shock therapy and prefrontal lobotomies are carried out on carefully selected patients after thorough appraisal of each case.

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Because there is a great demand for neuropsychiatric beds, every attempt is made to handle as many of these patients as possible through mental-hygiene clinics. Emphasis is placed upon rehabilitation of the neuropsychiatric patient with as early return as possible to normal living. General medical survey teams examine all patients in some of the Veterans Administration neuropsychiatric hospitals for evidence of intercurrent illness, and this has often led to unusual findings, which may be of fundamental significance. An example of this is the fact that prostatic hypertrophy in patients with chronic psychosis appears to be almost nonexistent.

In the field of tuberculosis many significant advances have been made. In approximately 25 of the Veterans Administration tuberculosis hospitals, one of the largest and best controlled studies in the use of streptomycin in the treatment of this disease has been carried out. The care of the tuberculous psychotic patient poses a major problem, which is receiving the benefits of a special program. Aseptic technic in the Veterans Administration tuberculosis hospitals has provided a model that many civilian institutions have followed. Complete registration of all tuberculosis patients has been established and will be maintained in co-operation with state health departments.

Unfortunately, applications for admission to tuberculosis hospitals operated by the Veterans Administration are far in excess of the number of beds available, and to meet this situation it has been necessary to utilize the facilities of practically every state, county and municipal sanatorium in the country. Consequently, building plans call for the construction of more tuberculosis hospitals.

One of the most important departments in Veterans Administration hospitals is medical rehabilitation. Many veterans, as a result of their disabilities, are no longer able to pursue the same type of job that they had prior to their illness or injury. This is particularly true in chronic cases, and programs are designed so that these veterans leave the hospital equipped to pursue a successful career in a new vocation. The dietetic department plays an important role because the Veterans Administration realizes that proper diet is important in treatment. In convalescent patients, it is as important as medication. Social-service workers assist veterans in meeting personal problems that might bar their progress toward health. During intervals when patients are not being subjected to diagnostic or therapeutic procedures, their time is no longer spent in idleness or boredom. This is where the special-services department plays a part. Chaplains to meet patients' spiritual needs and librarians to furnish reading material are available. In addition, recreational activities, entertainment, light athletics, movies and canteens are available for their benefit. Domiciliary homes are operated to care for veterans who are able to work a few hours a day, and who need a minimum amount of professional care. This enables the Veterans Administration to utilize the limited number of hospital beds in general hospitals to the greatest advantage.

Despite the outstanding progress that has been made in the medical care of the veterans, a number of criticisms has been directed at the program. Perhaps the most significant of these is its expense. In order to accomplish the objective of "medical services second to none" it has been necessary to depart from the old concept that federal hospitals, while operating in beautiful buildings, must maintain a per capita cost that provides little more than domiciliary care.[2] Good medical care is expensive. The cost is highest in teaching hospitals, largely because of the overhead associated with research and other activities intimately tied up with medical advances in the teaching program. However, to eliminate such activities would be to strike at the heart and soul of good teaching and medical progress.[3] The use of diagnostic procedures and improved technics has raised the cost of medical care but has contributed immeasurably to the efficiency of the entire program.

An indication of the cost of medical care is the duration of the individual patient's stay in the hospital. Here again, because of the number of patients with chronic cases who enter Veterans Administration hospitals, the over-all stay is somewhat longer than that encountered in civilian hospitals caring for more acute disease.[4] However, any notion that it takes longer to complete proper investigation of a patient in a Veterans Administration hospital than in a civilian hospital is erroneous. It is important to realize that prior to the institution of the present program, the average hospital stay of a general medical and surgical patient in a Veterans Administration hospital was thirty-seven days. At the present time this has been reduced to less than thirty days. When it is realized that the Veterans Administration hospitals are now carrying out surgical procedures of extraordinary magnitude that were not attempted in former times, this figure is all the more impressive. The average per diem cost of Veterans Administration patients in 1949 was $6.58 in neuropsychiatric hospitals, $12.72 in tuberculosis hospitals and $14.22 in general medical and surgical hospitals. These figures compare favorably with similar figures in nonveteran institutions throughout the country.

It has been argued that since the patient in the Veterans Administration hospital is not paying for his hospitalization he is not anxious to be discharged. This may be true in isolated cases but is not a factor of major importance. The fact is that cost of hospitalization is but one of many considerations that affect the patient while he is hospitalized. Most patients are faced with loss of income, interruption of schooling and separation from their families.

Any one or a combination of these factors constitutes an impelling reason why they are anxious to be discharged from the hospital at the earliest possible date.

A final factor that also influences the length of stay in Veterans Administration hospitals and is not generally appreciated by the public is the necessity for complete study within the hospital. Except for service-connected disability, the law does not permit outpatient care at the Government's expense, and accordingly, in many cases, it is necessary for a patient to enter the hospital for complete diagnostic study prior to operation. Also, because many veterans live at great distances from Veterans Administration hospitals, they must remain in the hospital until their convalescence has been completed.

Many people wonder why it is necessary to continue to build additional Veterans Administration hospitals. It is readily understandable when one considers the potential load of veterans eligible for hospital benefits within the next twenty-five years. A statistical summary released by the Veterans Administration on January 31, 1950, showed there were 19,035,000 living veterans, of whom 15,313,000 served in World War II, the difference representing veterans of World War I and other wars. From this it becomes obvious that a great number of eligible veterans will seek hospitalization within the next twenty-five years. Moreover, as the average age of the veteran increases, his need for hospitalization increases. Accordingly the peak load will not be reached until after 1970, when it will approach 250,000 beds. Ten years after World War I, there were 30,311 veterans hospitalized. In July, 1945, just prior to the end of World War II there were, 71,713 and on January 31, 1950, there were 112,332 patients in Veterans Administration hospitals. Long-range planning is required for this selection rather than a vacillating policy of adopting temporary expedients suggested by well meaning groups who are not always conversant with the facts.

Another criticism of the Veterans Administration is that it does not utilize existing Army or Navy hospitals that have been closed instead of building new institutions. In some instances this has been done, but in most cases it has not been found feasible. Many Army hospitals are located in isolated areas where it would be impossible to arrange a suitable affiliation with a medical school and it would be difficult to attract a full-time professional staff. Furthermore, many Army hospitals are of temporary or at best semipermanent construction, and their upkeep is excessively expensive. The majority of Army hospitals are also of a cantonment type, which requires extra personnel and thus adds to the operating expense.

Much has been said in recent months about the fact that a large percentage of veterans receiving care in Veterans Administration hospitals do not have service-connected disabilities or illnesses. In this respect the law is clear.[5] It provides that veterans with service-incurred or service-aggravated disabilities are entitled to hospital and outpatient care for those disabilities at Government expense. It also provides that veterans with nonservice-connected disabilities may be admitted to Veterans Administration hospitals or other Government hospitals provided a vacant bed is available and the patient signs a statement that he cannot afford to pay for care in a civilian hospital. The establishment of such eligibility for hospital care, of course, must be a legal determination. Once the patient is admitted, irrespective of whether he has established service-connection for his case or not, there can be only one standard of medical care, the best possible.

One aspect of the eligibility of the veteran with nonservice-connected disability for care requires special consideration. Most service-connected disabilities fall into rather limited groups and if Veterans Administration hospitals were limited to this type of patient it would be impossible for them to maintain well trained and competent staffs because of the limited variety of pathologic processes available for treatment and study. Indeed, this resulted after World War I, when the majority of Veterans Administration hospitals handled only service-connected diseases and it soon became impossible to recruit the best trained physicians and surgeons for these institutions. As a result the veteran with service-connected disability was not receiving the best medical care. From this point of view, then, the care of patients with nonservice-connected diseases in Veterans Administration hospitals is essential to the maintenance of a well-balanced patient distribution for the purposes of teaching and the attraction of competent medical and surgical staffs. The care of such patients is therefore an essential feature of good medical care for all veterans. Whether they should be required to pay in some measure for this care is a matter for the country to decide. At the present time no payment is required according to law.

It has been erroneously implied that the Veterans Administration operates independently and arbitrarily without the advice and assistance of the medical profession as a whole. A group of national consultants, representing all the medical and surgical specialties, meets approximately every two months at the Veterans Administration Central Office, Washington, D. C., to review the program and recommend changes for its improvement to the Chief Medical Director and his staff. Moreover, in the six area offices located throughout the country, in addition to a full-time staff, there are consultants in all the medical specialties. There are 59 area medical consultants in the various specialties attached to the Boston Area alone. These men make periodic surveys of the activities in their

respective specialties in the Veterans Administration installations in this area, and make recommendations for improvement.

At Veterans Administration hospitals, another group of consultant and attending physicians render direct service to the hospitals, making ward rounds, performing operations and participating in the training of residents. These hospital consultants and attendants serving at hospitals affiliated with medical schools are appointed by the deans' committees of the medical schools involved. Consultants appointed at hospitals not affiliated with medical schools are appointed upon the recommendation of the area consultant in the particular specialty involved.

The regional office medical clinics authorize treatment of service-connected cases by private practitioners of medicine on a fee basis. This enables the veteran to have free choice of a physician approved by the state medical society, either as a general practitioner or as a specialist. All treatments must be authorized in advance, except in cases of emergency. The majority of treatments are done by practicing physicians rather than by Veterans Administration staff physicians. In addition, prescriptions written by authorized physicians can be filled by local pharmacists, under a Veterans Administration home-town pharmacy plan. Also, by a cooperative plan, visiting-nurse associations and other community nursing services are authorized to render service on a fee basis to veterans with service-connected disabilities after discharge from Veterans Administration hospitals.

It would be difficult to conceive of any medical program with more active participation of specialists and private practitioners in medicine than that which now exists in the medical program of the Veterans Administration.

Many important preventive aspects of the program are being integrated in the various activities. The magnitude of the medical program can be appreciated when one considers that the Veterans Administration must deal with members of Congress, representatives of service organizations and medical societies, faculties of medical schools, practicing physicians, dentists and nurses, parents and relatives of veterans, as well as entitled veterans themselves.

Finally the Veterans Administration is aware of the fact that consideration must be given to the art as well as the science of medicine. Younger physicians are taught that they must consider a patient not only in relation to his illness but also in relation to his home, his family, his job, his hopes and his aspirations. They are reminded of the words of Sir William Osler[6] that we must be ever mindful of our vows as physicians, when we care for those unable to care for themselves, who in their hours of tribulation, need about them gentle hands and tender hearts.

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FIFTY YEARS OF MEDICAL PROGRESS

MEDICINE AS A SOCIAL INSTRUMENT: TROPICAL MEDICINE

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BEFORE undertaking to evaluate the progress that has been made in tropical medicine during the first half of the twentieth century, one should explore the content of this commonly accepted field of medicine. A simple definition based on climate or geography would give a false idea of the concept of tropical medicine as it has been built up in textbooks, graduate schools and professional parlance to include the study, prevention and treatment of a wide range of diseases found within the tropics and to a large extent outside. What, then, are the criteria that today determine the inclusion of diseases among those commonly designated as tropical and therefore of special concern to tropical medicine?

Among the criteria for classification as tropical disease climate may first be considered. The most characteristically tropical climate is warm and humid. And yet, for various reasons, diseases that prevail in the dry heat of the subdesert, like oriental sore, or exist in the cool air of high valleys in the Andes, like verruga peruana, or even flourish best in cold winter seasons in the temperate zone, like typhus fever, are currently included among the tropical diseases. Why?

The quality of being exotic is important among the characteristics that now qualify diseases as tropical. Under the impact of civilization and its expression through preventive medicine, sanitation and a higher standard of living, many diseases like typhus, leprosy and smallpox have largely disappeared from the more advanced countries of the temperate zones. These diseases are still entrenched in distant foreign countries, which sometimes happen to be in the tropics but are often merely far away, in the egocentric view of the world taken by scientific medicine. Many other diseases may be expected to become "tropical" as they are exiled from favored areas, unless they are banished at the same time from the now underdeveloped countries.

Another factor determining inclusion among the tropical diseases is the property of being transmitted to man by insects, ticks or mites. In some cases the lower animals — for example, rodents and monkeys — are the reservoirs of the infection that insects and ticks transmit to man, but the outstanding characteristic of a large and important group is arthropod transmission.

It is customary to lump together the human diseases caused by animal parasites, especially the worms and protozoa, and include them with the tropical diseases. This is quite natural considering the relatively undisturbed prevalence of such parasites in the tropics, as well as in underdeveloped areas elsewhere.

This ends the listing of criteria of tropical diseases. There are others, but these seem to be the most important, and in various combinations they explain why almost any one of the traditional tropical diseases has acquired its classification.

The specialty of tropical medicine has justified itself by its utility to a particularly interested group, just as industrial and military medicine are important to other groups. The development of the teaching of tropical medicine has in the past been promoted primarily for the purpose of preparing medical personnel for posts in colonies, for assignment to military or missionary stations, for service in connection with foreign commercial, agricultural or research projects, and for scientific or military expeditions. But quite as important a reason for its development has been the desire to call attention to medical subjects relatively neglected in medical schools in the temperate zone, and thus to round out the body of local medical knowledge and to make possible the recognition and treatment of diseases that are locally uncommon.

This specialty, in addition to its interest in tropical diseases as defined, takes into consideration the effects of complex foreign environments on any disease and on health. Increasingly it has taken into account the ecology of disease vectors and hosts and of man himself in any of the surroundings called tropical. In this discussion tropical medicine is considered to include related phases of public health, parasitology, pharmacology and sanitation, and even the all-important social and economic factors.

AGENTS CAUSING TROPICAL DISEASES

The present century opened in the heyday of the ardent search for the microbial causes of disease, and the successes in the field of tropical medicine had already been many. But there remained important maladies whose etiology was in total darkness, and still others whose known agents later revealed such important characteristics or

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novel stages of development as to justify consideration here.

At the very beginning of the century the nature of the causal agent of yellow fever was revealed in Cuba by the United States Army Yellow Fever Commission headed by Walter Reed. In October, 1901, the diluted blood serum of a yellow-fever patient was filtered through a new Berkefeld cylinder, and the resulting filtrate was injected into 3 soldier volunteers. All 3 came down with yellow fever. The cause was thus shown to be a filterable virus, and yellow fever became the first human disease to be attributed to this class of agents.

Before the period covered by this discussion the species of plasmodium responsible for the three common kinds of human malaria were well known, as seen in anopheles mosquitoes and in the blood of man. There remained, however, an important gap in the developmental cycle that was filled only toward the end of the half-century. It was not known where and in what form the parasites existed between the injection of the sporozoites by the mosquito and the appearance of the organism in the blood at the end of the incubation period. Moreover, no one had ascertained the location or state of the plasmodium between an acute attack and a relapse. Finally the discovery of the missing stages of the incubation period was reported by Shortt to the Fourth International Congresses on Tropical Medicine and Malaria in Washington in 1948. Exhaustive microscopical search for the missing forms had been made in the tissues of rhesus monkeys that had been bitten repeatedly by enormous numbers of anopheles mosquitoes infected with a monkey-malaria parasite, *Plasmodium cynomolgi*. The infection was reinforced by the injection of the ground-up bodies of the mosquitoes. From the fifth day after inoculation till the tenth, when the incubation period was ending, a large new form of the plasmodium in various stages of development was found in the parenchymatous cells of the liver. To relate the new knowledge to human malaria, a volunteer was subjected to infective bites as the monkeys had been, but this time it was by over 2000 anopheles infected with *P. vivax* of human source. In addition the salivary glands of 200 of the infected mosquitoes were injected intravenously to increase the magnitude of the infection. On the seventh day a piece of liver was removed by operation, and in it were found pre-erythrocytic forms of the plasmodium similar to those seen in the monkey livers at the same interval after inoculation. Later, a similar experiment with another volunteer revealed in the liver cells corresponding forms of *P. falciparum*.

These are two of the spectacular discoveries of this period, one at the beginning and the other at the end. Between were many others relating to causal agents, but only a few of the more important ones are mentioned here. The agent of African sleeping sickness, *Trypanosoma gambiense*, was discovered in man in 1901. The organisms of kala-azar, *Leishmania donovani*, and oriental sore, *L. tropica*, were first identified in 1903. *L. braziliensis* was found in 1909 to be the cause of the mucocutaneous leishmaniasis of South America.

The cause of typhus fever, *Rickettsia prowazeki*, was first described in 1910. The rickettsia of scrub typhus or tsutsugamushi, *R. orientalis* (*R. nipponica*) was first seen in 1920. The cause of Carrión's disease, including its forms Oroya fever and verruga peruana, was found in 1905 to be a rickettsia-like organism, *Bartonella bacilliformis*.

The organism causing yaws was discovered in 1905 and named *Treponema pertenue*. Pinta was long believed to be an infection with fungi, but in 1938 a spirochete, *T. carateum*, was found to be the cause. The causal agents of dengue, the viral encephalitides and trachoma were found to be filterable viruses. Sprue, beriberi and pellagra, previously considered due to infection, were properly classed as nutritional-deficiency diseases.

Discovery and Conquest of Tropical-Disease Vectors

A dramatic discovery significant for tropical-disease control was made at the very threshold of the present century and rightfully belongs both to the century in which it was made and to the one in which it was reported and applied. When "twenty-four buglers in concert" were sounding taps at Columbia Barracks in Cuba for the old year 1900 and the closing century, Walter Reed in his historic letter to his wife was expressing thanks to God that it had been permitted to him and his assistants on the Army Yellow Fever Commission to "lift the impenetrable veil that has surrounded the causation of this most wonderful, dreadful pest of humanity," yellow fever. On the preceding Christmas Day his experiment to clinch the evidence for mosquito transmission had given an unequivocal result. A soldier volunteer who had submitted to the bites of *Aedes aegypti* mosquitoes that had previously bitten yellow-fever patients came down with unquestioned yellow fever, whereas other subjects who had stayed in the same hut on the other side of a mosquito-proof screen remained in good health.

The bugles were sounding taps also for a long era of uncontrollable epidemics of yellow fever in the United States and elsewhere, since the application of the long-sought information was prompt and effective. Gorgas eliminated the disease from Havana, which had been a focus and distributing point for over a century. Later, he cleared the Canal Zone of yellow fever through mosquito control. Several important cities were promptly freed.

Encouraged by the uniform success in the eradication of yellow fever from cities and its disappearance from the surrounding countrysides, Gorgas, in

1914, evolved his key-center theory and interested the International Health Board of the Rockefeller Foundation in making an attempt to eradicate yellow fever from the world. This was to be done through the suppression of the domestic tropical mosquito, *Aedes aegypti*, in the limited number of large cities in which the disease was able to maintain itself. The first attack on the entrenched disease was in Guayaquil, Ecuador, in 1918. Within six months the disease had been permanently eliminated there. In northeast Brazil it later became evident that yellow fever could not always be so easily exterminated, and that there must be unknown factors that had not been taken into account. In 1927 the West African Yellow Fever Commission of the Rockefeller Foundation discovered that the common rhesus monkey was even more susceptible than man to yellow fever and could be used as a subject for experiments. In 1930 Theiler, at Harvard Medical School, showed that mice could also be infected if inoculated intracerebrally. With these laboratory animals available the possibilities of laboratory and field investigation were greatly increased. In 1933 Soper and his associates, working in Brazil, found that yellow fever was being transmitted to man by species of forest-dwelling mosquitoes in the complete absence of *A. aegypti*. This important discovery banished the hope of the early extermination of yellow fever through the suppression of *A. aegypti* breeding in key cities. It was soon found by blood tests in mice that men and various species of monkeys in the tropical forests of South America and Africa had acquired immunity. Yellow fever in man contracted through the bites of forest mosquitoes was designated as jungle yellow fever, sometimes called sylvatic.

Protection tests of many thousands of human serum specimens collected in a world-wide survey, and the examination of liver tissue from persons who had died of brief acute illnesses in regions of interest, revealed that there were great previously unsuspected areas in the tropical zones of Africa and South America where infection was constantly present in monkeys and was occasionally transmitted to man. The virus in such regions was actually isolated from wild-caught forest mosquitoes in Africa and South America and from captured sick marmosets in Brazil.

In the latter years of the half-century the ecologic studies of the animal hosts and forest mosquito vectors of yellow fever were intensified on both continents. The mosquitoes and monkeys of the upper levels of the tropical forest were found to be particularly well suited to the role of perpetuating the virus. They formed a permanent reservoir from which the disease could occasionally emerge to start aegypti-transmitted epidemics in towns and cities. Figure 1 shows one of the methods used in ecological studies of the mosquito vectors of jungle yellow fever. Men serving both as bait and as collectors are stationed in the forest on the ground and at two levels in the trees to capture the mosquitoes that come to bite them. This picture was taken during a study of the entomologic aspects of an outbreak of jungle yellow fever in man in the Republic of Panama in 1948 and 1949.

With the proved existence of large reservoir areas of yellow fever it became doubly important to keep

FIGURE 1. *Capturing Mosquitoes with Human Bait at Different Levels of the Forest in Entomologic Studies of Jungle Yellow Fever (Reproduced from Galindo, P., Trapido, H., and Carpenter, S. J. Observations on Diurnal Forest Mosquitoes in Relation to Sylvan Yellow Fever in Panama.* Am. J. Trop. Med. **30**:533-574, *1950, with the Permission of the Gorgas Memorial Laboratory and the Publishers).*

towns and cities noninfectible. By perfection of organization and technic governmental authorities have been able to exterminate *A. aegypti* from entire countries of South America, and an international drive to eliminate this dangerous mosquito from the Americas is being sponsored by the Pan American Sanitary Bureau. In this the countries are now helped by the availability of DDT as a residual house spray, which is effective against the urban vector of yellow fever as well as the anopheles that transmit malaria. Nevertheless the attack on the *A. aegypti* larvae in water receptacles in houses is

still the most economical method of separate vector control, but the containers are being sprayed with DDT instead of being treated with oil as formerly.

To the last years of the previous century belong the epoch-making discoveries of Ronald Ross, which began in 1897 and were supplemented by those of Grassi. These discoveries established the transmission of malaria by anopheles mosquitoes. The practical application to malaria control belongs definitely to the half-century now ending.

The early methods of malaria control were drainage and filling of anopheles breeding places, oiling of water surfaces to kill the larvae or the introduction of fish. These methods were expensive and

FIGURE 2. *Dipping in a Roadside Pool in Sardinia for the Larvae and Characteristic Eggs of* Anopheles labranchiae (*Courtesy of the Rockefeller Foundation*).

therefore inapplicable to many rural areas. Where there was special governmental or commercial interest or a sufficiently dense and thrifty population there was marked success. In 1901 Watson pioneered in this field by organizing a successful malaria-control program in Malaya. A few years later Gorgas and Le Prince reduced malaria to an insignificant amount in the Panama Canal Zone.

A considerable reduction in the cost of widespread malaria control was obtained in 1921, when Barber and Hayne introduced the use of Paris green for destroying anopheles larvae. This poisonous powder, diluted with an inert dust, was spread on water surfaces by hand, by mechanical blowers or from airplanes, and the anopheles larvae swept the lethal particles into their mouths.

Then came the attack on the imago or adult mosquito. In 1933 Park Ross began the weekly spraying of native huts in Zululand with pyrethrum insecticide and accomplished a marked reduction in malaria at low cost. Sprays were used increasingly to disinsect not only homes but also the airplanes, which threatened to spread anopheles and other dangerous insects to new fields.

An advance of the first magnitude was ushered in by the startling discovery in 1943 of the extreme potency of DDT (dichloro-diphenyl-trichloroethane) as an insecticide and its low toxicity for man. These properties were discovered by the Bureau of Entomology and Plant Quarantine of the United States Department of Agriculture in the course of a search for more effective insecticides for use in killing lice to prevent typhus in the world war. When applied to malaria control this substance revealed properties beyond fondest hopes, and was found useful for destroying both larvae and adult anopheles. Sprayed on the interior walls of buildings this nonvolatile crystalline chemical remained for many months, acting as a contact poison on any alighting insects. In many countries the systematic use of DDT at infrequent intervals as a residual spray in all dwellings has brought malaria under control and sometimes close to extermination at a reasonable cost. Incidentally, it has destroyed many insects other than anopheles: mosquitoes, sand flies, bedbugs and house flies.

In the early days of malaria control Watson and Darling advocated singling out the most dangerous local species of anopheles for control and ignoring the others. This method was called species sanitation. More recently malariologists were puzzled by the unexplained absence of malaria in certain regions in which anopheles were abundant. In 1931 Hackett and other investigators became interested in an earlier academic observation of Falleroni that the species *Anopheles maculipennis* could be subdivided into a number of races by the distinctive markings on their eggs. Seven such races have been recognized and named. The profound differences in their ability to transmit malaria explained the observed anophelism without malaria. To species sanitation was added subspecies or race sanitation, and control became more discriminating and effective.

The investigation and control of anopheles mosquitoes required numerous studies of anopheles and their larvae and of their ecology in each malarious region. In Figure 2 an entomologist and his assistant are dipping for the larvae and eggs of *A. labranchiae*, a dangerous member of the maculipennis complex.

Encouraged by the successes in eliminating *Aedes aegypti* from large areas Soper and Wilson in 1939 attempted the eradication of *Anopheles gambiae* from Brazil. This extremely efficient malaria vector had been accidentally introduced from Africa to Natal, Brazil, in 1930, and in nine years it had spread about 300 miles to the northwest, occupying 1200 square miles and causing devastating malaria epidemics. The Government of Brazil and the International Health Division of the Rockefeller Foundation combined forces in the effort, and at one time about 2000 persons were engaged in this urgent attempt to stop the invader and prevent its spread to a large part of the continent. The

application of Paris green as a larvicide and the use of pyrethrum spray for disinsecting houses and vehicles resulted in complete extermination in less than two years.

In 1942 *A. gambiae* was again on the march. In southern Egypt there was a sudden and virulent outbreak of malaria due to an invasion of gambiae down the Nile Valley. The Government of Egypt invited the Rockefeller Foundation to direct its gambiae eradication campaign, and in 1944 Soper was put in charge. Larvae were destroyed by the use of Paris green, and adult mosquitoes in houses were killed with pyrethrum spray. A residual spray of DDT was applied to railroad cars and river boats. By February, 1945, gambiae could no longer be found in Egypt.

An opportunity to attempt the extermination of an indigenous malaria-bearing anopheles presented itself in the highly malarious island of Sardinia. From 1946 to the middle of the century a field experiment was carried on by the Government of Italy with the co-operation at first of UNRRA and later of the Economic Cooperation Administration and under the direction of experts from the Rockefeller Foundation. The object was to exterminate *A. labranchiae*, the only established vector of malaria on this large island. When the planned campaign was ending in 1950, malaria had been completely eradicated, but a few labranchiae were still being found, and the original main objective had not been attained.

The culmination of malaria control in the United States is the five-year National Malaria Eradication Program of the state health departments and the United States Public Health Service. It was launched on July 1, 1947, and should be completed by the middle of 1952, except for three subsequent years of watchful observation. Efforts are concentrated on indoor spraying with DDT, by the method illustrated in Figure 3. In the seven most malarious states of the thirteen classed as malarious, the number of cases of primary malaria has already fallen so low that it is evident that only sporadic cases are occurring and that the disease is fast disappearing.

That typhus fever is transmitted by the body louse was shown experimentally by Nicolle, Conte and Conseil in Tunis in 1909. As a preventive of typhus wholesale bathing and disinsecting of clothes was practiced during and after the first world war, with limited effect, since the methods did not prevent reinfestation. The discovery of the powerful and lasting insecticidal powers of DDT in the second world war made it possible for the military and UNRRA and the local authorities to prevent the repetition of the extreme typhus epidemics that had occurred in Serbia and Poland during or after the first world war. For example, UNRRA rushed 100 tons of 10 per cent DDT powder to Poland for civilian use and taught the recently devised simple method of dusting subjects without the removal of clothing. As a result typhus outbreaks after the second world war were brief and almost negligible in Poland. Similar results were obtained elsewhere.

The detailed knowledge of the rodent hosts of plague and of the flea vectors has been developed within the period under review. Sylvatic plague in various wild rodents has been discovered, studied and mapped. Examination of rodents and more recently the more delicate method of testing their fleas for plague bacilli have greatly extended the known reservoir areas. Early attempts to eliminate plague through the extermination of the wild rodent hosts fell short of their goal. The methods for plague control in populous places and seaports through rat destruction and elimination of rat harborage in buildings and ships have been highly successful. The direct attack on the rat flea by blowing DDT dust into rat holes has recently come into use and has removed the danger that rapid destruction of rats during an epidemic would increase human infections.

FIGURE 3. *Operator Spraying Walls with DDT Solution in the Campaign to Eradicate Malaria in the United States (Courtesy of the Communicable Disease Center, United States Public Health Service).*

The transmission of African sleeping sickness or trypanosomiasis by tsetse flies, species of glossina, was recognized early in the century. In later years the disease has been confined and diminished by the vigorous and systematic application of large-scale measures directed against the vector and also against the human infection. Trees have been cleared from the banks of streams to interfere with tsetse breeding, whole villages have been removed to fly-free areas, and all human inhabitants have been barred from large infected tracts. In some

areas the disease in man has been reduced, and the chance of infecting tsetse flies diminished by periodic inspection of all the inhabitants and the treatment of those with trypanosomes in their enlarged cervical lymph nodes. Studies of the various tsetse flies carrying infection to man and domestic animals have been intensified in the hope of finding ways to control them more widely and thereby to open up large parts of Africa to fuller development.

The important role of phlebotomus species, or sand flies, in transmitting tropical diseases, especially kala-azar, Oroya fever and pappataci fever was determined after the beginning of the century. New hope has been raised that these insects can be controlled by the systematic spraying of houses with DDT, for Hertig has reported that in Greece this procedure, aimed at malaria, has brought about a profound reduction in sand flies.

Helminths in Tropical Medicine

The old-world hookworm disease, due to *Ancylostoma duodenale*, was known long before the period covered in this review but the new-world species, *Necator americanus*, was not described until 1902. The complex route of invasion of the human body from larva-infested soil through the skin, blood vessels and lungs to the intestines was discovered by Looss in Egypt in 1904. The new parasite, like its previously known relative, drew blood from the intestinal walls and produced anemia as the outstanding symptom. Historically, ancylostomiasis is of especial interest as the first disease to be attacked through a well financed and organized international campaign. This activity began in 1909, when the Rockefeller Sanitary Commission was established to combat hookworm disease in the southern part of the United States, and developed into an international effort in 1914, when the International Health Board of the Rockefeller Foundation took over the work and extended it to many countries. Through sanitation to prevent soil pollution and through treatment of infected persons to remove their worms, health was improved, and the ground laid for better public-health organization. Vigorous attempts at complete eradication of hookworm infection by these methods failed even in isolated islands, doubtless because of the difficulty of removing the last worms through any justifiable intensity of treatment and the then unexplainable tendency of the infection rates and worm burden to rise toward their former equilibrium after treatments had stopped.

In relation to these international campaigns and accompanying studies, Cort and his associates, experimenting with *Ancylostoma caninum* in dogs, showed that in slowly acquired infestations antibodies that limited further acquisition of worms were formed. Working with the same hookworm infection in dogs in 1935, Foster and Cort demonstrated that a deficient diet reduced this power to acquire immunity against superinfection, and that the resumption of an adequate diet restored it. This suggested that the observed extreme human hookworm infections encountered in certain areas and the low equilibrium of infection in other equally, insanitary places might well be determined by differences in diet.

The futile attempts at eradication were given up, and emphasis was placed on sanitation and the treatment only of persons with significant worm infestation and related symptoms. In most places the hookworm problem has been diminishing steadily with improvement in general conditions and a great increase in the wearing of shoes.

Bilharziasis, or schistosomiasis, caused by three species of flukes, is an important cause of disease and disability in vast areas of Asia, Africa and South America. The chances for control were greatly increased from 1913 to 1918 by the unraveling of the life histories of the parasites encountered in Japan and Egypt, and the identification of species of fresh-water snails that acted as intermediate hosts. The destruction of these snails by periodic removal of vegetation from canals and the killing of snails and cercariae with copper sulfate has brought relief in parts of Egypt, but the employment of these measures on a large enough scale is still considered impracticable. Education to prevent water pollution presents still greater difficulties.

Prevention through Vaccination

Many methods of immunization of varying degrees of effectiveness have come increasingly into use. For an outstanding example of substantial progress in control through vaccination one cannot do better than turn to yellow fever. After animals became available for experiments in 1927 many unavoidable illnesses and deaths from yellow fever occurred among scientists exposed to virus-laden materials. Then followed the discovery of the vast yellow-fever reservoirs in monkeys and uncontrollable forest mosquitoes. Vaccination of persons under risk of jungle yellow fever or laboratory infection seemed the only possible solution of the problems presented.

A satisfactory method of vaccination was reached by stages in the laboratories of the International Health Division of the Rockefeller Foundation. In 1931 Sawyer, Kitchen and Lloyd brought the series of laboratory infections to an end by immunizing personnel with simultaneous injections of mouse-adapted neurotropic virus of greatly lowered viscerotropism and enough human immune serum to protect against encephalitis. This effective but cumbersome method could not be applied to enough people, and in 1936 it was superseded by the use of a virus strain of extremely low virulence, 17D, derived by Lloyd, Theiler and Ricci, and Theiler and Smith from the virulent pantropic Asibi strain by

prolonged cultivation in chick embryo tissues in vitro. This culture virus was multiplied in living chick embryos, and the processed pulp was dried in the frozen state for distribution. Many millions of persons — military personnel of the second world war, travelers through infected regions and inhabitants of jungle-yellow-fever areas — were immunized by single subcutaneous injections of this living vaccine. By analysis of field experience and by blood tests it was shown that nearly all vaccinated persons were immune for at least six years after inoculation, and in 1949 the yellow-fever panel of the World Health Organization recommended that certificates of inoculation be recognized as valid for quarantine purposes from the tenth day tc the end of the sixth year. This method ranks with vaccination against smallpox in the certainty, solidity and duration of the immunity produced, and it is superior in respect to reaction, since there is no lesion at the site of inoculation and since there have been only the mildest of general reactions since 1942, when the danger of serum hepatitis was removed by the exclusion of normal human serum from the process of manufacture.

In French West Africa there is unquestioned need for periodic universal vaccination of the 16,000,000 inhabitants against both yellow fever and smallpox. Separate subcutaneous inoculation against yellow fever on so large a scale seemed impracticable. Accordingly, Peltier and his associates devised a method by which a mixture containing dried neurotropic yellow-fever virus and also vaccinia virus is applied to the scarified skin of the arm. An even higher degree of yellow-fever immunity is obtained than with the 17D strain inoculated subcutaneously, and the vaccinia lesion develops in the usual way and is followed by satisfactory immunity. By 1948, 20,000,000 vaccinations had been performed, 17,000,000 by the combined method and 3,000,000 against yellow fever alone. Ease of administration, low expense, and satisfactory immunity had been obtained but at the cost of occasional late meningeal symptoms and rarely of frank encephalitis. Experiments have been initiated at the Yellow Fever Research Institute at Lagos to determine whether the relatively avirulent 17D strain can be substituted for the neurotropic virus in the above methods without too great a loss in immunizing power and without the disconcerting complications.

Chemotherapy and Antibiotics

The effectiveness of tropical medicine has been strikingly augmented in recent years by the advances in chemotherapy and the spectacular development of antibiotics. In malaria there have been two great stimulating factors: the exigencies of warfare in highly malarious areas with the source of quinine cut off, and the appreciated need for drugs that would really cure malaria by attacking not only the parasites in the blood but also the tissue phases of the incubation period and of the interval between illness and relapse. The first of the important synthetic antimalarial drugs was plasmoquine, introduced in 1928, which was unique in its destructive effect on the sexual forms of the parasite in the blood, but was handicapped by rather high toxicity. Atabrine (quinacrine) became available in 1933, and was successfully used during the second world war to suppress malaria in exposed troops and for treating soldiers and civilians. Like quinine the more active Atabrine was effective against the asexual parasites in the blood but did not destroy the exo-erythrocytic forms responsible for relapses. Within the past decade other drugs have become available that are even more effective than Atabrine, notably chloroquine and Paludrine, but no safe drug has yet been obtained that can completely eradicate the tissue form in vivax malaria, thereby eliminating relapses.

A great advance in therapy came in 1935 with the discovery of the sulfonamides, and during the war certain of them proved highly efficacious in the treatment of bacillary dysentery in the troops. Sulfonamides have been used with beneficial results also in the treatment of plague, but the antibiotic streptomycin proved to be even more effective. New hope has been given the victims of leprosy, for the old, relatively ineffective chaulmoogra-oil treatment is giving way to the use of sulfones, which regularly produce slow but definite improvement. A quick-acting drug is still needed.

For the treatment of amebic dysentery the use of the alkaloid emetine began in 1912, and it is still considered the most valuable single drug for this disease. Since then, many effective synthetic products have become available, some of them organic arsenicals and others in the oxyquinoline series. Various compounds have been prepared for the treatment of bilharziasis, the filarial diseases, kala-azar and trypanosomiasis. Many of them are arsenic or antimony preparations of limited effectiveness and high toxicity. Nevertheless, treatment has definitely improved, and there is great activity in the synthesis and testing of new drugs.

In the last decade of the half-century antibiotics came strongly into the picture, beginning with the advent of penicillin as a therapeutic agent. In the mass treatment of yaws neoarsphenamine is being superseded by the even more effectual penicillin. The present campaign for the eradication of yaws from Haiti, carried on by the World Health Organization with the co-operation of the United Nations International Children's Emergency Fund and the Government, is based on the use of penicillin.

Really effective treatment became available for rickettsial disease in 1948, when Smadel announced the effects of chloramphenicol (Chloromycetin) on scrub typhus in Malaya. This drug, and another

antibiotic, aureomycin, bring scrub typhus promptly under control through their rickettsiostatic effect, and any relapses may be similarly controlled.

Tropical Medicine As a Social Instrument

The various scientific accomplishments discussed above are obviously having their immediate beneficial effect for the well-being of mankind. Nevertheless, an occasional voice is raised to protest that the very successes are heading a crowded world toward misery and disaster by rapidly increasing the population. To be sure, this attack could have been directed also against scientific agriculture, which multiplies population by increasing the food supply, and also against effective government, which maintains peace. All will agree that the answer is not a return of high infant mortality and unrestrained infectious disease, aided by famine and war. The remedy increasingly advocated is to raise the standards of living, education and health, which experience has shown reduces high birth rates.

But the application of scientific medical knowledge to individual countries and local communities is not the outstanding service of tropical medicine to mankind. Its special place is in international health. The geographic areas of greatest interest to tropical medicine are the underdeveloped regions. These are just the places where shortcomings in economics, agriculture, education and health keep countries at the sort of disadvantage that breeds discontent and leads to conflict. There is now a belated realization that great differences in status between countries in these respects are a world hazard.

Early in the half-century it was surmised that improvement in health would promptly be followed by increased production, and a better economic position would result in fuller social development. Probably, the health work would have had this effect except for the periodic setbacks by war and by interference with international trade, travel and communications. The problem is much broader than health, which cannot flourish in an adverse socioeconomic environment.

International tropical medicine received an impulse in 1914, when the Rockefeller Foundation began its activities in the prevention of hookworm disease, malaria and yellow fever in tropical countries, and in building up their health departments and training their experts. Subsequently governments have come to the realization that assistance in health activities can be a potent factor in improving international relations. Support for such activities has been forthcoming from governmental sources, but the setbacks have been serious. The fine program of the Health Organization of the League of Nations came to an end when the League succumbed after its failure to enforce peace. The Health Division of UNRRA in its short life placed great emphasis on emergency tropical-disease control and the restoration of governmental health services. The World Health Organization has made a splendid start with a larger and broader program than that of any of its predecessors, but has been weakened by the withdrawal—temporary, it is hoped—of several countries of eastern Europe.

The use of tropical medicine as an instrument for achieving peace is well illustrated by the position of the United States. The foreign policy is concerned with removing the basic causes of world unrest. The steps the Government is taking include efforts to improve world health through the World Health Organization and also through co-operation with individual governments.

Only failure to prevent devastating war can stop the advance in international health. But given abiding peace tropical medicine can indeed function effectively as an instrument of social progress.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

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CASE 37061

PRESENTATION OF CASE

A forty-five-year-old man was admitted to the Emergency Ward because of fever, malaise and anorexia.

The illness began with epigastric pain following a feast of corn bread and "spirits" four days prior to admission. The next day he noted coryza, sore throat, a nonproductive cough and mild fever. Two days prior to admission the cough became productive of white, tenacious sputum, and he noted enlarged tender cervical lymph nodes. The symptoms increased in severity, and on the morning of admission he ached "everywhere." He had anorexia, and had eaten little during the four days of illness. He came to the hospital because he lived alone and had no one to care for him.

There was a history of nocturia three to four times nightly and "nervousness." He had many illnesses over the past thirty years, having been admitted to this hospital on thirteen previous occasions for various complaints during the past eleven years. He had had malaria twenty-seven years before entry, a penile lesion two years later (the year that he entered this country) and gonorrhea the next year. Nineteen years before admission he was treated for pulmonary tuberculosis in a sanatorium for six years. The tuberculosis was considered inactive at that time, and there was no subsequent evidence of activity. The right upper lobe was fibrotic. He incurred minor contusions of the right leg in an automobile accident thirteen years before entry. Following that, he developed thrombophlebitis and, two months later, chest pain and bloody sputum, which persisted for two weeks. Twelve years prior to entry he visited Greece, where his wife was living, and contracted "Spanish influenza." This disease was manifested largely by chest pain and fever, and subsided after a few weeks. He was first seen at this hospital eleven years before admission because of thrombophlebitis of the veins in both lower extremities. At this time serological tests for syphilis were positive, and he was started on a prolonged course of therapy, including arsphenamine. In the following years there were several recurrences of the thrombophlebitis, and finally, four years prior to entry, bilateral saphenous vein ligations were done. The blood pressure and cardiac findings were always within normal limits. The first recorded blood pressure was 100 systolic, 70 diastolic. Three years before entry he had several "fainting spells," during one of which he bit his tongue and was incontinent of urine. An accurate description of those episodes could not be obtained, but a diagnosis of epilepsy was considered probable. The spinal fluid Wassermann and Hinton tests were negative. The patient was started on dilantin sodium, and no further episodes occurred. Sixteen months prior to admission he was seen in the Medical and Neurology Clinics three times over a one-week period because of severe occipital headaches of two months' duration. The only significant new finding was the rise of the blood pressure from the previous normal level to 178 systolic, 104 diastolic. There were no murmurs or other evidence of cardiac abnormalities. There were no positive neurological findings. A urine examination was negative. He was advised to return for further study but was not seen again until the present admission.

Physical examination showed a somewhat lethargic man, who appeared acutely ill. The venous pattern over the lower extremities was prominent, and there was + ankle edema. The posterior pharynx was slightly injected. There were several palpable, firm, movable cervical lymph nodes on both sides. Examination of the chest disclosed diminished breath sounds on the right, with a few moist rales at the right apex. The mediastinum was shifted slightly to the right. The point of maximum cardiac impulse was between the midclavicular line and the left sternal border. There was a Grade II to III diastolic murmur in the aortic area, heard along the sternum and downward to the left toward the apex. The rhythm was regular. The abdominal examination disclosed slightly increased resistance in the right upper quadrant. The neurologic examination was negative.

The temperature was 103°F. rectally, the pulse 120 and the respirations 20. The blood pressure was 120 systolic, 60 diastolic, but the sounds did not completely fade out until 20.

The urine was normal. Examination of the blood disclosed a hemoglobin of 14.0 gm. and a leukocyte count of 12,200, with 50 per cent segmented neutrophils, 4 per cent band forms, 36 per cent lymphocytes, 8 per cent monocytes and 2 per cent eosino-

phils. The stools were guaiac negative, and a throat smear showed a few gram-negative and gram-positive bacilli. A sputum examination showed no acid-fast bacilli. Roentgenographic studies of the chest showed no important change from previous studies. The entire right lung field was reduced in size and contained numerous emphysematous blebs. The upper lobe was reduced in size more than the other lobes. The heart did not appear unusual; the aorta was somewhat dilated and tortuous. The left lung was unchanged.

On the second hospital day the temperature rose slightly and a Grade III systolic murmur was heard in addition to the diastolic murmur. The patient's condition was otherwise unchanged. The temperature dropped to 101°F. rectally on the third hospital day, but he continued to have multiple complaints, including nausea, abdominal pain and tenderness and "nerves." He was transferred to a medical ward for further study.

A physical examination made at that time disclosed no significant changes from the previous one. However, during the course of the examination, he was suddenly seized with a pain which began in the neck and descended to the abdomen. Following this he felt "weak," and belched several times. He appeared somewhat cyanotic, and the pulse was weak, thready and irregular. He then made several efforts to vomit. Following this, the pulse was stronger, with only occasional extrasystoles. The blood pressure was 110 systolic, 40 diastolic. He complained of pain in the left lower abdomen and requested an enema. Shortly afterward he appeared to improve; he seemed to have much less distress, complaining only of numbness in the left leg. Neurologic examination of the lower extremities disclosed no abnormalities. The femoral pulse could not be palpated on the left, but was strong on the right. However, there was no evidence of circulatory impairment of the leg. During the next seven hours he complained occasionally of vague precordial pain, but his condition appeared essentially unchanged from that of the previous day. A urine examination showed a + test for albumin but was otherwise normal. The blood hemoglobin was 14.5 gm., and the leukocyte count 7400, with 50 per cent segmented neutrophils, 4 per cent bands, 28 per cent lymphocytes, 14 per cent monocytes, 2 per cent eosinophils and 2 per cent early forms thought to be myelocytes.

Seven hours after the episode of pain described above, the patient complained of severe precordial pain, but this time there was no radiation. On physical examination, the cardiac murmur previously heard showed no change. While the examiner was auscultating the lung field posteriorly, the patient suddenly slumped back, complained of precordial pain and said "I think that I am going out." He then closed his eyes and began a series of enormous respiratory gasps. The nails and lips became cyanotic, and the face a brownish red. The pulse was not palpable, and no heart sounds could be elicited by auscultation. However, he continued to gasp at intervals for another moment or two. The pupils were dilated and did not react to light. The left was slightly larger than the right. Oxygen and an intracardiac injection of epinephrine were given, but with no appreciable effect. The respiratory efforts ceased, and the patient was pronounced dead.

Differential Diagnosis

Dr. F. Dennette Adams*: Before starting my discussion of this case, I should like to take a moment to pay tribute to the unsung heroes in Dr. Mallory's department who write these protocols. The record of any patient with multiple admissions to this hospital is necessarily two to three inches thick. To wade through such a mass of material, cull out the essentials, clarify one's thoughts, and write such a succinct and well ordered summary as this one, is a time-consuming, difficult and thankless task. The residents to whom the job is assigned from week to week have my admiration.

For those of you who were not around at the time, it might be well to record that "Spanish influenza" was the name given to the severe respiratory infection that killed so many persons in the epidemic of 1918–19. The early cases appeared in Spain; for several years thereafter the Spaniards were blamed for what happened later.

The patient had malaria at the age of eighteen. Since there is no suggestion of any recurrence, one can discount this disease as a possible factor in the final illness. At twenty he had what one may assume, because of later blood tests, was a primary lesion of syphilis, and from twenty-six to thirty-two he was hospitalized with tuberculosis. Either of these may be pertinent to the terminal illness. Within a short time following discharge from the tuberculosis sanatorium came his first attack of thrombophlebitis. From then on, he had repeated attacks. The chest pain and bloody sputum that developed following the initial episode may well have been indications of pulmonary infarction. Perhaps, too, the chest pain and fever that occurred a year or so later while he was in Greece could be attributed to the same cause. They could have represented pneumonia — or, less likely, a reactivation of the tuberculosis.

At thirty-four, thrombophlebitis appeared as the cause of the first admission to this hospital. Further attacks occurred thereafter. Meanwhile, he was treated for syphilis because of the history and the positive blood tests. At that time the heart was reported as normal.

The spells of unconsciousness that began at forty-two cannot be explained. One can only state that a diagnosis of "idiopathic" epilepsy is hazardous

*Physician, Massachusetts General Hospital.

when the trouble begins as late in life as forty-two. At the time, one should have been most suspicious of brain tumor, a tuberculoma or some intracranial luetic lesion. Nor can one find a satisfactory explanation for the severe headaches that occurred at forty-three. In my experience, what one might call run-of-the-mill hypertension is not a common cause of headaches. They do occur during the course of a rapidly developing hypertension, during a hypertensive crisis and with excessively high blood pressure. But one rarely sees high blood pressure as a cause when the systolic readings are not above 180 to 200 or the diastolic not over 120. To find the reason for headache is often difficult. A careful history, a clear-cut understanding of the various headache patterns, and often a large number of investigative procedures are necessary. To discuss the various possibilities here would be a digression. Dr. Castleman, was a blood Hinton test done at this time?

DR. BENJAMIN CASTLEMAN: The Hinton and Wassermann tests were both positive about one and a half years before the final admission.

DR. ADAMS: He reverted from a negative blood back to a positive blood. That may be of importance.

Now I reach the final admission. He entered the hospital with the picture of severe upper respiratory infection. He was apparently sicker than one would expect with ordinary "grippe." Physical examination showed signs consistent with fibrosis of the right lung, diminished breath sounds, a few rales, and a shift of the mediastinum to the right. A Grade II to III diastolic murmur in the aortic area and downward along the sternum is recorded, but nothing is said about a systolic murmur. If this observation was correct, it will have a distinct bearing on my final diagnosis. Such a diastolic murmur in a patient known to be luetic is characteristic of syphilitic aortic-valve insufficiency. But it would be most unusual to have a diastolic murmur loud enough to be rated Grade II or III without any accompanying aortic systolic murmur. Occasionally a murmur will spring up overnight, the most likely cause being rupture of a valve leaflet or rapid development of a large vegetation.

A STUDENT: I saw this patient that night, and he did have a systolic murmur at that time, as well as the diastolic murmur.

DR. ADAMS: Thank you. That statement tends to lead me away from one diagnosis that I had in mind, makes another less likely and would add support to that of syphilitic aortitis with aortic valvulitis. Dr. Castleman, were any blood cultures taken?

DR. CASTLEMAN: None are recorded.

DR. ADAMS: May we now see the x-ray films?

DR. JAMES J. MCCORT: We have films of the chest taken almost yearly for nine years before the final admission. I shall use the films taken when the patient was thirty-eight years of age for comparison. These early films show almost complete collapse of the right upper lobe. There is considerable thickening of the pleura over the entire right lung. Compensatory emphysema, and probably bleb formation, are present in the right lower lobe. The mediastinum is shifted to the right side. A small calcified nodule can be seen in the superior segment of the right lower lobe. The left lung is entirely clear. The heart is not enlarged. There is a slight prominence of the aortic arch.

DR. ADAMS: The aorta is widened?

DR. MCCORT: I do not believe it is in the examination made when he was thirty-seven years old. The films taken in the last admission, when the patient was forty-four years old, show that the right lung has not changed. There is collapse of the right upper lobe, compensatory emphysema of the right lower lobe and thick pleura over the entire right lung. The heart is much larger, and this enlargement appears to be mainly in the region of the left ventricle. On the lateral film you will note there is some increase in size internally, which also suggests possible slight enlargement of the right ventricle. The aorta is now elongated and tortuous and may be slightly dilated in comparison with the previous examination. The width of the pulmonary artery has increased in the seven years between the examinations. The pulmonary vascular markings are accentuated.

DR. ADAMS: The changes in the heart and aorta also tend to support a diagnosis of syphilitic aortitis.

So I am now ready to assume that at the time of his final admission he had chronic inactive tuberculosis, syphilitic aortitis with aortic valvulitis and a recent acute infection.

The next problem is: Why did he die — and die suddenly? Before I learned, as I did a moment ago, that a systolic murmur was present on admission — and before Dr. McCort's demonstration of the x-ray films, I considered the bare possibility of acute tuberculous pericarditis, with the pericardial rub being mistaken for murmurs. On one occasion, in a patient with known mediastinal and cervical lymphadenitis, I saw tuberculous pericarditis develop abruptly and cause death within a few days. The onset and symptoms were similar to myocardial infarction, and that diagnosis was made clinically. It was changed at autopsy. In the patient now under discussion, I need not regard the murmurs as having been confused with a rub; and there is such good evidence for aortitis that acute tuberculosis can be dismissed.

Another diagnosis that must be considered is that of a Herxheimer reaction, resulting from possible use of an antibiotic for the acute infection that precipitated his hospitalization. If he had syphilitic aortitis, one could postulate increase of obstruction at the mouth of a coronary artery by

the use of penicillin or some other antibiotic. Was he given antibiotics following admission?

A STUDENT: He did not receive antibiotics.

DR. ADAMS: That information would seem to exclude this diagnosis, which at best would be unlikely.

What about acute bacterial endocarditis superimposed on an already damaged valve? Had that systolic murmur developed suddenly, it might well have been due to perforation of a leaflet, or sudden change in size of a valvular thrombotic lesion. But we now know that the murmur was there at the start; so this bit of evidence is no longer tenable. One could postulate also that arterial emboli thrown off from the acute diseased aortic valve might have accounted for some of the more distant symptoms, such as the interference of circulation in the leg and the abdominal pain. But this disease can be strongly suspected only if peripheral emboli can be proved, or if a positive blood culture is obtained. So one can only speculate that it might have been present.

Because the first episode began in the neck, extended downward and involved both the abdomen and the left leg, one must seriously consider rupture of the aorta due to syphilitic aneurysm or, more likely, the dissecting aneurysm seen in the nonsyphilitic aorta caused by necrosis of the media. The character of the pain would be more suggestive of the latter, especially since it extended down into the leg. On the other hand, if one believes, as I do, that the man had syphilitic aortitis it would seem unwise to introduce the added diagnosis of perforation due to medial necrosis. Against dissecting aneurysm is also the fact that there was no urinary shutdown. I believe that there is a more tenable explanation. Recall, if you will, that the two acute episodes of pain occurred during physical examinations; the second began while the lungs were being examined. This latter attack, occurring a few hours after the first episode, was characterized by precordial pain and some degree of cyanosis. No mention is made of distention of neck veins, which would be expected either with extensive pulmonary embolism or with acute cardiac tamponade due to rupture of the aorta. In spite of this I believe, for two reasons, that pulmonary embolism was the most likely cause of death. First, the patient falls into the group which Loewe[1] has labeled thrombophils. We have a story of repeated attacks of thrombophlebitis over a period of thirteen years. With this background there is every reason to suppose that he could have another attack of thrombophlebitis during the course of the current acute infection. Furthermore, with one attack of pain he felt distended and requested an enema. We know that serious pulmonary embolism is often associated with the feeling of abdominal distention and a call for the bedpan. Secondly, both the episodes occurred while he was being examined, and in the case of the second the statement is made that it occurred while his lungs were being auscultated. Years ago I learned from Dr. Irving S. Wright, and he later wrote,[2] that in the presence of thrombophlebotic disease, active examination of the lungs is unwise. Increase of the negative thoracic pressure created by deep inspiration favors the dislodgment of a clot.

My final diagnoses, therefore, are: syphilitic aortitis with aortic valvulitis, acute respiratory infection, multiple pulmonary embolism secondary to thrombophlebitis, old inactive pulmonary tuberculosis and acute bacterial endocarditis.

A PHYSICIAN: He had had a ligation.

DR. ADAMS: The saphenous veins had been ligated; thrombophlebitis can just as well occur in other veins.

DR. ALLEN G. BRAILEY: This man's heart action ceased abruptly. If he died of pulmonary embolism, would you not expect the cardiac function to have failed less suddenly?

DR. ADAMS: I cannot answer that.

DR. ALFRED KRANES: It may be of some importance that about a year before the final admission no diastolic murmur was heard. One might therefore assume that it was of relatively recent vintage. If that is so, your argument for luetic aortitis is on less firm ground. The diagnosis of ruptured dissecting aneurysm is somewhat more likely.

DR. ADAMS: I too thought of that, and meant to mention it. My reasoning was that the diastolic murmur of early aortic insufficiency is a hard one to hear and is often missed on routine examination. I hazarded the guess that he may have had a soft diastolic murmur at the examination sixteen months prior to the final admission, but that it was not discovered.

A PHYSICIAN: I should like to ask Dr. Adams how he accounted for the absence of a femoral pulse.

DR. ADAMS: If one presupposes thrombophlebitis, one could presuppose spasm of the artery. The change in the femoral pulse also was one of the important findings that suggested to me the possibility of acute bacterial endocarditis.

CLINICAL DIAGNOSES

Syphilitic aortitis, with deformity of aortic valve.
Cardiac arrhythmia.

DR. ADAMS'S DIAGNOSES

Syphilitic aortitis with aortic valvulitis.
Acute respiratory infection.
Multiple pulmonary emboli secondary to thrombophlebitis.
Old inactive tuberculosis.
?Acute bacterial endocarditis.

ANATOMICAL DIAGNOSES

Dissecting aneurysm of the aorta, ruptured, with cardiac tamponade.
Cardiac hypertrophy, hypertensive type.

Pathological Discussion

Dr. Castleman: The autopsy showed a large heart that weighed 520 gm. and was quite characteristic of the hypertensive type of hypertrophy. The left wall was quite thick. The aortic valve was normal. There was no evidence of syphilis or rheumatic infection. The cause of death was a rupture of a dissecting aneurysm of the aorta into the pericardium, with tamponade. The dissection had descended as far as the bifurcation of the aorta in the abdomen. The clinical correlation is somewhat hard to reconstruct, because the attack of pain came after the murmur. Ordinarily, when one thinks of a murmur associated with a dissecting aortic aneurysm, one assumes it is probably due to the intimal tear flapping about near the aortic valve. The intimal tear was just 1 cm. above the valve. I suppose one has to assume that at first the patient had the tear with a localized medial hematoma, and that the severe pain seven hours before death was due to the dissection.

Dr. Kranes: The illness did start out with epigastric pain.

Dr. Castleman: Yes; but it seemed to disappear, and it sounded more like an infection. We found no real evidence of infection, although I believe he had a mild upper respiratory infection. There were a few polymorphonuclear leukocytes in some of the alveoli, but I do not believe it amounted to much. He did have the old disease that showed in the x-ray films — a collapsed fibrotic upper lobe and pleuritis with the emphysema nearby. There was no anatomic evidence that he had had syphilis.

A Physician: What did the orifices of the renal arteries look like?

Dr. Castleman: They were not occluded by the dissection. None of the major branches of the aorta were occluded. I think the clue to the correct diagnosis was that the murmur was not heard a year before.

Dr. McCort: Was there any evidence of pulmonary infarction?

Dr. Castleman: No; there was so much scarring, however, that it is possible that some of the scars were due to old infarcts.

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Case 37062

Presentation of Case

A sixty-eight-year-old man entered the hospital for evaluation of an x-ray shadow in the lung.

One and a half years prior to admission he had a "virus" infection characterized by fever, tinnitus, and a cough productive of thick yellow sputum. The episode lasted one week, and an x-ray film of the chest showed "infection." Four months previously he experienced a similar episode that was treated with Chloromycetin and that subsided in a week's time. Three follow-up x-ray films, however, over a one-month period, showed a persistent hilar shadow. He entered another hospital, where a diagnosis of lung tumor was made by x-ray. Bronchoscopic examination was negative there, but cytological examination of the sputum was said to be positive for malignant cells.

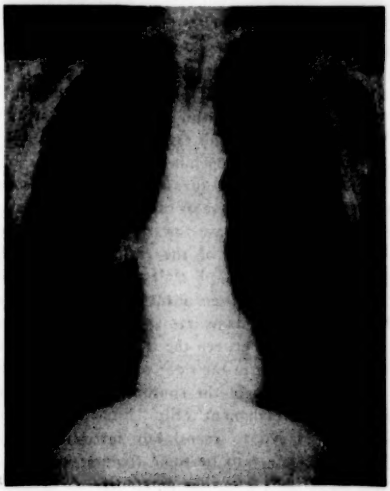

Figure 1.

Other than during his bouts of "virus infection" the patient had been free of cough. There had been no recent weight loss, hemoptysis or chest pain.

Four years before admission a combined abdominoperineal resection of a cancer of the rectum was performed. Fourteen lymph nodes examined microscopically were negative. Except for increasing exertional dyspnea, especially during the six months before entry, the past history was noncontributory. Until two months prior to admission he had smoked one package of cigarettes a day.

Physical examination showed a well developed and well nourished man, who appeared younger than his stated age. Decreased tactile fremitus and slight dullness over the left posterior chest were observed. Breath sounds on the right were loud and bronchovesicular. The right diaphragm was elevated 2.5 cm. The abdomen was normal except for a low mid-

line scar, which contained a colostomy opening. There was an anal pouch that admitted the fingertip.

The temperature, pulse and respirations were normal. The blood pressure was 150 systolic, 82 diastolic in the right arm and 136 systolic, 80 diastolic in the left arm.

The urine was normal. The serum nonprotein nitrogen, sodium and chloride, and the prothrombin time were normal. An electrocardiogram was within normal limits. An x-ray examination of the chest showed a mass measuring 6 by 4.5 by 8.5 cm. lying in the anterior segment of the right upper lobe, which bulged the medial portion of the minor septum downward (Fig. 1). This extended far back toward the lung root. The bronchus to the right upper lobe was not well seen on any film. There was some atelectasis close to this mass superiorly. The esophagus appeared to deviate toward the left and posteriorly at the level of the carina. There were probably enlarged lymph nodes at the bifurcation, but no other nodes were identified with certainty. The mass lay in immediate apposition to the anterior chest wall between the third and fourth ribs. No fluid was seen in the right pleural space. Cytologic examination of the sputum was reported as doubtful for malignant cells. Bronchoscopic examination failed to reveal any intrinsic masses. There did appear to be some compression of the right upper-lobe bronchus anteriorly. A cytologic examination of bronchial washings was reported as doubtful.

On the sixth hospital day an operation was performed.

Differential Diagnosis

Dr. Arthur S. Pier, Jr.*: In summary, this sixty-eight-year-old man had a large asymptomatic mass involving the upper lobe of the right lung, and the problem is a differential diagnosis of that mass. I think that we might look first at the x-ray films.

Dr. Stanley M. Wyman: We are fortunate in having some previous films of this man's chest, taken at another hospital. They extend back three years before admission, at which time no appreciable disease was present. The remainder of these outside films, taken a month apart three years later, show in the lateral view an indefinite mass in the anterior segment of the right upper lobe, with a second distinct smaller nodule in the right third interspace that is seen on both examinations, so that there are apparently two distinct lesions in the lobe. The examination made here two months later shows the major mass in the right upper lobe to have increased still further in size in the anterior segment, and it is well seen in immediate contact with the chest wall at this point. The displacement of the esophagus is seen in the left anterior oblique projection, suggesting the presence of a node anterior to and on the right side of the esophagus.

Dr. Pier: Is the diaphragm much elevated on the right?

Dr. Wyman: I think that if anything the diaphragm lies lower than usual. The patient may have some emphysema.

Dr. Pier: Do you see much collapse in the lung?

Dr. Wyman: There is some atelectasis in the upper lobe, adjacent to the lesion, but no significant collapse of the lobe otherwise.

Dr. Pier: One of the first questions that occurs is whether this man's disease represents infection or tumor. There is certainly very little evidence in the history to suggest an infectious process. He had no fever, his pulse was normal, he felt well, he had lost no weight and I assume the blood studies were normal; I cannot conceive of his having a lung abscess or empyema, nor do I think there is any likelihood of a tuberculous process in a man of this age who has been asymptomatic until relatively recently. Sometimes a virus pneumonia can give rise to considerable atelectasis, which will give a very suspicious shadow, lasting occasionally for months, that often has us greatly worried. Here, however, the process seems to be growing.

I think that in a man of sixty-eight years I do not need to consider too seriously certain congenital conditions, such as dermoid cysts, teratomas or bronchogenic cysts. I think he had a tumor involving the lung. I think in a man of this age, with tumor in the lung, the chances are very strong that it was a malignant process and not a benign one. The history spoke of the diaphragm's being elevated. It would be interesting to know whether on fluoroscopy the right diaphragm moved. If it did not move, I should suppose the phrenic nerve was involved. Such involvement would be further evidence of a malignant process. If his disease were on the left

*Assistant in medicine, Massachusetts General Hospital.

side, it might also affect the left recurrent laryngeal nerve, giving rise to hoarseness, which would be corroborative evidence of a malignant process. Since this lesion was located on the right, we do not have that clue.

If the patient had a malignant tumor, what are the possibilities? He had an operation for carcinoma of the rectum four years previously, and apparently two tumor masses were found in the lung at the present examination. The possibility of metastases from the old cancer must be considered. It seems to me that such advanced and far-flung metastatic involvement would be very unlikely in a man who has felt well, who has lost no weight and who apparently had a negative abdominal examination. I should expect a carcinoma of the rectum to metastasize first to the liver. Also, if the carcinoma had gone this far to the lung I should expect a considerably debilitated patient. I think I shall assume that he did not have a metastatic process. I think a lymphoma is also very unlikely. A lymphoma of this extent and degree would probably give rise to the mediastinal symptoms of venous obstruction, with distention of the veins in the arms, and so on. It does not look like a lymphoma to me on the x-ray films.

I think he probably had a primary lung tumor. Squamous-cell bronchogenic carcinoma or the oat-cell type would most likely have given rise to cough. He had no cough. Also I think that the chances are good that these tumors would be seen on bronchoscopy. The tumor he most likely would have, with no story of cough and a negative bronchoscopy, would be an adenocarcinoma arising in a small bronchial radicle. Adenocarcinomas often can grow very large without being symptomatic. I saw a man in the hospital the other day who had an inoperable adenocarcinoma; he had no chest symptoms at all other than a slight degree of dyspnea. I shall make a diagnosis of adenocarcinoma of the right upper lobe. I think some weight should be attached to the sputum positive for malignant cells at the other hospital.

Dr. Edward B. Benedict: The only bronchoscopic evidence that he had a tumor was pressure on the right upper-lobe bronchus, and we thought that was very likely due to a malignant tumor, probably carcinoma. We could not see any evidence of inoperability: that is, the carina was not fixed or widened, and the bronchus was not fixed. We thought he ought to be explored surgically to establish the diagnosis.

Dr. Allen G. Brailey: Does Dr. Pier think the second nodule was a metastasis from the original carcinoma?

Dr. Pier: Yes, from what I take to be a primary lung adenocarcinoma.

Dr. Gordon Scannell: We were not sure that this man did not have a metastatic carcinoma, but we believed the likelihood of a primary carcinoma of the lung was great and that he should be so treated. We therefore explored him.

Clinical Diagnosis

Primary carcinoma of the lung.

Dr. Pier's Diagnosis

Primary adenocarcinoma of the lung.

Anatomical Diagnosis

Metastatic adenocarcinoma of lung, from intestine.

Pathological Discussion

Dr. Scannell: When the chest was opened a mass in the anterior segment of the upper lobe was revealed as Dr. Pier predicted and the x-ray films bear out, although actually it invaded the superior aspect of the middle lobe to which the upper lobe was anatomically fused. In order to resect it, we were committed to an upper and middle lobectomy. In addition to the mass in the lung, we found that he had large lymph nodes in the mediastinum; a particularly large one was in front of and above the trachea — an unusual place for a lymph-node extension from a pulmonary tumor, especially when the lymph nodes in the right paratracheal chain were not involved. There was a large lymph node beneath the carina that was not fixed and did not give the characteristic distortion at bronchoscopy that goes with an inoperable carcinoma of the lung. The lymph nodes were quite discrete, and there was no obvious zone of carcinoma permeating from one to the other. We biopsied one of these and were given a report of adenocarcinoma on frozen-section examination. Since adenocarcinoma may be pri-

mary in the lung, we carried out a right upper and middle lobectomy; the man was not a good risk, and we wished to conserve as much lung tissue as possible. At the end of the operation we discovered that the small nodule that had been described in the upper lobe was in the apex of the lower lobe. It was removed with a wedge resection.

DR. BENJAMIN CASTLEMAN: When we dissected the lung we discovered that the upper lobe was not involved at all and that all the disease was in the middle lobe. The bronchus to the lateral segment of the middle lobe was full of tumor that was contiguous with tumor in the surrounding parenchyma. Most of the middle lobe was gray abnormal tissue, which microscopically was seen to be chronic pneumonitis secondary to the obstruction, but in addition there were foci of adenocarcinoma of the type that is quite characteristic of an intestinal tumor. The nodule in the apex of the lower lobe was also a metastasis. We are quite sure that this was metastatic from the adenocarcinoma of the rectum, even though metastases to the bronchi are not too common. Some years ago Dr. Donald King and I* looked them up in this hospital and found that in about 100 cases of metastatic disease to the lung about 20 per cent involved the bronchus; in about 6 or 7 of those we could actually see tumor within the bronchus. This is unusual in carcinoma and more common in sarcomas. What probably happens is that there is a metastasis to the parenchyma or to a lymph node, which then invades the bronchial wall; I believe that occurred here. This case reminds me of one that Dr. Edward Churchill had some years ago. He removed a lobe that looked microscopically exactly like this from a woman who had had a carcinoma of the rectum resected six years before. She remained well for eight years after the lobectomy and then died of cerebral metastases.

DR. BENEDICT: Were there any metastases elsewhere?

DR. CASTLEMAN: We do not know. This was a surgical specimen.

DR. SCANNELL: I think the mediastinal lymph nodes very likely contained tumor that was metastatic from the bowel, as the lung lesion was.

It might be worth while to mention that the prognosis following resection of a solitary metastasis of the lung after that length of time is really quite good.

DR. BENEDICT: It is not so good as for a solitary metastasis from a hypernephroma!

DR. SCANNELL: No; but it is as good as or better than that for a primary tumor of the lung, if there is a long period after the original resection and it is a "solitary" metastasis.

*King, D. S., and Castleman, B. Bronchial involvement in metastatic pulmonary malignancy. *J. Thoracic Surg.* 12:305-315, 1943.

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THE FUTURE OF THE VETERANS ADMINISTRATION MEDICAL PROGRAM

The precipitate resignation of Dr. Paul B. Magnuson as chief medical director of the Department of Medicine and Surgery in the Veterans Administration has occasioned grave concern among all who are interested in the medical care of the veteran, particularly as he has stated in a letter to all doctors in the Department of Medicine and Surgery, that "there was too much interference in the running of hospitals and the authority for running hospitals."

This is a serious indictment. The issues involved can be appreciated only against the background of progress that has characterized the medical program of the Veterans Administration in recent years.

In the Spring of 1945 in Frankfort, Germany, the commanding general of the United States Ground Forces convened with the chief surgeon of the European Theater of Operations and his chief consultant to discuss the future medical care of veterans of the United States Army. It was May, the war in Europe was over and although Japan was still to be conquered the future seemed full of hope and idealism. Under these propitious circumstances a complete reorganization of the Veterans Administration medical program was envisioned. To replace the archaic and bureaucratic system that had made veterans' hospitals places to be shunned, they planned a decentralized organization not unlike the Army's medical services in the European Theater where the care of the patient took precedence over all other considerations and where hospitals vied with each other for excellence. To make such a program an enduring one, they conceived the idea of linking it to those most stable of human institutions, the universities.

The ensuing years saw much of this concept come to fruition. Congress passed Public Law 293, which freed professional personnel from the restrictions of Civil Service Regulations. The universities supported the plan and took under their guidance the "affiliated hospitals." The names of Omar Bradley, Paul R. Hawley, Paul B. Magnuson, Elliott C. Cutler and Edward Cushing were identified with what Dr. Carroll, elsewhere in this issue of the *Journal*, has called "a transformation without parallel in the medical history of this country." Distinguished men in all branches of medicine were happy to serve, often at considerable personal sacrifice, as advisers and consultants. The medical and nursing staffs of Veterans Administration hospitals were brought to a par with the best civilian institutions, equipment was improved, opportunities for research were created and the veteran was provided with "medical care second to none."

All this was not accomplished without a struggle. As Dr. Carroll points out, there is much that has been criticized. No system is without fault, and the inherent defect in the Department of Medicine and Surgery in the Veterans Administration is that it is subject to the restrictions, regulations and budgetary limitations that affect the entire Veterans

Administration Program. Consequently, its personnel, its supplies and equipment and even its planning may be impaired by measures directed primarily toward abuses in other departments of the Veterans Administration. This defect was recognized at the outset by General Hawley. Complete rapport between him and General Omar Bradley minimized the problem, but with the departure of these men to other fields, the difficulties have slowly multiplied. Without warning, extensive reductions in personnel have been ordered, with results often deleterious to the care of patients; personnel ceilings have been established when certain hospitals were already seriously shorthanded, thus permanently crippling their staffs; minimal expenditures that would permit the development of research programs have been forbidden, while millions of dollars were being spent to erect hospitals where they were not badly needed.

Recognizing these defects, Dr. Magnuson has vigorously championed the cause of a more independently administered medical program. Under his leadership, substantial progress has been made in effecting affiliations between medical schools and the Veterans Administration hospitals. He has attracted the highest type of medical personnel to the Veterans Administration, and under him the best and most modern treatment of the incapacitated veteran has been assured. His insistence that the administration of hospitals and clinics should be under the direct control of the chief medical director has received the complete and unwavering support of his board of national consultants. Any deviation from his policies undoubtedly will bring about a deterioration in the medical program of the Veterans Administration. His loss is a grievous one; his successor assumes a momentous responsibility for the future of the program.

Fortunately, the appointment of Vice Admiral Joel T. Boone as chief medical director indicates that there will be no change in policy and no acceptance of lower standards. Admiral Boone, a holder of the Distinguished Service Cross and the Congressional Medal of Honor, a naval officer of distinction and a man of the highest personal integrity, is well equipped to maintain the high ideals and high standards of medical care originally envisaged by Generals Bradley and Hawley. In his efforts he will have the wholehearted support not only of his colleagues within the Veterans Administration but of the entire medical profession.

The ultimate future of the Department of Medicine and Surgery in the Veterans Administration, however, depends upon whether or not it is granted the autonomy it needs to manage its hospitals and clinics in accordance with the best medical traditions.

POUND BILL

A NEW bill has been filed in the House of Representatives of the General Court of Massachusetts that is designed to aid medical investigation into the nature and cure of the diseases that afflict humanity.

This bill, filed by Representative Louis K. Nathanson of the twelfth Suffolk District and sponsored by the Massachusetts Society for Medical Research, takes the place of the famous Nolen–Miles Pound Bill, which failed of passage in 1948. Its purpose is to furnish to qualified and licensed laboratories, for scientific experimental purposes, those stray cats and dogs that have been impounded in accordance with the present statute for a period sufficient to justify the assumption that they have been abandoned by their owners, if any, and would otherwise be legally executed.

The Massachusetts Society for Medical Research is the new corporate entity that has taken over the functions of the Massachusetts Committee for Medical Research. Under the presidency of Dr. John F. Conlin, director of medical information and education of the Massachusetts Medical Society, it represents Boston University School of Medicine, Harvard Medical School and Tufts College Medical School, those Massachusetts institutions that will suffer most in their educational and humanitarian enterprises from a lack of suitable laboratory animals.

Similar pound laws, after being referred to the voters, have been enacted in Baltimore and Los Angeles, despite vociferous and intemperate opposition. They exemplify the most practical and economical way by which laboratory animals can be procured for the service of humanity.

It is not to be expected that any headway can be made in overcoming the prejudices of those zealots who continually oppose the advances achieved by scientific medicine through animal experimentation. Their minds are inalterably set; efforts in this direction are wasted.

It is of the utmost importance, however, that the open minds of the uninitiated should be protected against the attempts at thought control that are made by the members of this cult, for their methods, although more hysterical, are as unprincipled as are those of communism, and departures from the truth represent no barrier to their utterances.

Every physician must be on the alert to combat the strategy of the antivivisectionists from now until House Bill No. 1101 is voted on. He must warn his friends and patients in general, and his legislators in particular against their tactics, for the opponents of the bill will come wrapped in coats of mink and shod in the hides of cattle, with the feathers of butchered birds in their hats, to plead that dumb animals should be executed for no useful end, rather than serve first the altruistic purposes of the most humanitarian of sciences.

Their appeal is to the emotions rather than to reason, and it is not based on facts. It must be countered with an appeal to the intelligence of the public — an appeal that must be based only on the simple truth.

INFLUENZA

Since the great influenza epidemic of 1918, every report of an extensive outbreak of grippe-like infections arouses the fear of a recurrence of the great morbidity and mortality that accompanied that pandemic scourge. However, although there have been moderately extensive outbreaks of influenza-like infections in 1928 and 1933 and small outbreaks in several of the intervening years, none have had the characteristics of the 1918 disease. Since 1933, furthermore, each of the epidemics has been traced to a virus that has been recognized as either influenza A or influenza B, or to variants of these viruses. The underlying cause of the influenza of 1918 has never been determined; the deaths during that pandemic were associated with various bacterial complications in the lungs. The pneumonias accompanying the more recent outbreaks, on the other hand, have not been of unusual severity, nor have they been associated with unusually high mortality.

In recent weeks, as on many similar occasions in previous years, reports from foreign countries have come through press and radio concerning high morbidity rates and unexpectedly large numbers of deaths from what is called influenza. These have come mostly from northern Germany, Great Britain and the Scandinavian countries. The best information suggests that the excessive numbers of deaths are occurring only among the aged and infirm and not among the young and previously healthy, as was the case in 1918. There are also indications that the viruses causing influenza in these areas are related to the influenza A virus.

It is possible that the extent and severity of these European outbreaks are connected with the fact that influenza has not been highly prevalent in these areas in recent years. Some outbreaks of influenza have been recognized in several parts of the United States during the last three years. It is not expected, therefore, that any outbreak that may occur in this country will be of unusual extent or severity, or that it will differ materially from the outbreaks of this disease that have been recognized since 1933.

It should be borne in mind, moreover, that because of the availability of potent antibacterial agents much of the mortality from influenza and perhaps much of the severe and prolonged morbidity can be prevented by early and intensive treatment of bacterial complications. Antibiotics, however, should not be used routinely for all mild cases of the grippe — and most cases in any epidemic of influenza are very mild.

The antibiotics should be used in all severe cases and in patients in whom pulmonary complications are observed or suspected. In such cases the antibiotics should be used in full therapeutic doses. The choice of the agent will depend on the prevalent bacteria found in the respiratory flora of the severe cases.

As to the efficacy of vaccination against influenza viral infections, the experiences of the past few years have been varied and unpredictable. This has been due largely to the appearance of variants of the virus that were immunologically distinct from the strains used in the preparation of the available vaccines. It is not possible to prepare vaccines from the virus of the present European outbreak in time for them to be used effectively or to have any important influence on the influenza that may occur this winter. Widespread vaccination with the presently available vaccines is, therefore, not to be recommended.

THE LABORATORY TECHNOLOGIST

THE shortage of properly qualified medical technologists, not only in Massachusetts but elsewhere, should be a matter of grave concern to all physicians. Elsewhere in this issue of the *Journal* is a résumé of a panel on the subject, which was sponsored by a committee appointed by the Central Health Council and presented at the Massachusetts Medical Society meeting last May and before the Massachusetts Hospital Association last month.

The papers read at the panel, as well as the remarks that followed from the floor, made it perfectly clear that, although many hospital laboratories do high-grade work, the work of others is at times distressingly inadequate. Indeed, each year the number of technicians trained at substandard schools of medical technology exceeds the number graduating from schools approved by the American Medical Association. The inadequately trained technologist, often working in a small hospital with little or no supervision by a pathologist, is soon confronted with technical tests beyond her ability, and wrong results are bound to follow. Some of these mistakes have seriously affected treatment of the patient.

The problem concerns the medical profession as a whole, and the pathologists and technologists need the help of all physicians. A much larger number of technologists must have education in basic sciences at the college level for effective understanding of the technical procedures and must have their technical training in schools approved by the American Medical Association and the Registry of Medical Technologists of the American Society of Clinical Pathologists.

The supply of qualified medical technologists could be increased if their financial returns were reasonably adequate. Hospital trustees, directors and medical staffs should consider the possibility that the qualified medical technologist, who can perform her work accurately, is indeed a better investment than the lower-paid person who does less work — and too much of it inaccurately.

In the Provincial Surgical and Medical Journal, is the report of a case of a boy, who actually swallowed a silk handkerchief nearly a foot square. On the third day it was dejected from the bowels, perfect in every respect, except a slight discoloration. Probably this is the first instance in which a human subject has been thoroughly wiped out with a silk handkerchief.

Boston M. & S. J., *February 12, 1851*

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

CARRIGAN — Paul W. Carrigan, M.D., formerly of Boston, died on December 20. He was in his fifty-fourth year.

Dr. Carrigan received his degree from Tufts College Medical School in 1924. At the time of his death he was a commander in the Medical Corps, United States Navy. He was a fellow of the American Medical Association.

Three sisters, a brother and a nephew, Dr. Walter Carrigan, survive.

HOGAN — Joseph A. Hogan, M.D., of Lawrence, died recently. He was in his seventy-ninth year.

Dr. Hogan received his degree from Harvard Medical School in 1897.

Two sisters survive.

HOLT — Edward W. A. Holt, M.D., of North Andover, died on October 28. He was in his seventy-second year.

Dr. Holt received his degree from Harvard Medical School in 1903. He was physician of the Board of Health of North Andover for thirty years.

Two sons and two daughters survive.

CORRESPONDENCE

BRAIN SURGERY THREE HUNDRED YEARS AGO

To the Editor: In my researches into early American history incident to a search for material on penology in Massachusetts, I came across an account of what may well have been the first brain operation in America.

The author of the account, the Reverend Increase Mather, Congregational minister, author, diplomat and president of Harvard College, was one of the most brilliant and influential men of his time in seventeenth-century America. He is reputed to have been "the author of ninety-two distinct works, besides many learned and useful prefaces." Before he was twenty-one he had mastered the Old Testament in Hebrew and the New Testament in Greek. With an intense desire to explain the mysteries of life he had written extensively in the fields of religion and philosophy, sharing with his contemporaries and with his famous son, the Reverend Cotton Mather, minister of the North Church in Boston, the current belief in witchcraft. Intrigued with the esoteric and the unusual, he collected in book form a number of stories of remarkable happenings in the Massachusetts Bay Colony. This book (*Remarkable Providences Illustrative of the Earlier Days of American Colonisation*) was written in 1683 and 1684, just prior to his assuming the office of president of Harvard College. There he describes in detail an operation — if it can be called that — that might have been the first on the brain in America. He does not tell the exact date of the event, but it must have occurred about the middle of the century or before. The operation is described as follows:

Remarkable was the preservation and restoration which the gracious providence of God vouchsafed to Abigail Eliot, the daughter of elder Eliot, of Boston, in New England; concerning whom, a near and precious relative of hers informs me, that when she was a child about five years old, playing with other children under a cart, an iron hinge, being sharp at the lower end, happened to strike her head, between the right ear and the crown of her head, and pierced into the skull and brain. The child making an outcry, the mother came, and immediately drew out the iron, and thereupon some of the brains of her child, which stuck to the iron, and other bits, were scattered on her forehead. Able chyrurgeons were sent for — in special Mr. Oliver and Mr. Prat. The head being uncovered, there appeared just upon the place where the iron pierced the skull, a bunch as big as a small egg. A question arose, whether the skin should not be cut and dilated from the orifice of the wound to the swelling, and so take it away. This Mr. Prat inclined unto, but Mr. Oliver opposed, pleading that then the air would get to the brain, and the child would presently die. Mr. Oliver was desired to undertake the cure; and thus was his operation:- He gently drove the soft matter of the bunch into the wound, and pressed so much out as well he could; there came forth about a spoonful; the matter which came forth was brains and blood (some curdles of brain were white and not stained with blood): so did he apply a plaister. The skull wasted where it was pierced to the bigness of a half-crown piece of silver or more. The skin was exceeding tender, so that a silver plate, like the skull, was always kept in the place to defend it from any touch or injury. The brains of the child did swell and swage according to the tides:—when it was spring-tide her brain would heave up the tender skin, and fill the place sometimes; when it was neap-tide, they would be sunk and fallen within the skull. This child lived to be the mother of two children; and (which is marvellous) she was not by this wound made defective in her memory or understanding.

EDWIN POWERS
6 Parker Street
Lexington, Massachusetts

BOOK REVIEW

Normal Values in Clinical Medicine. By F. William Sunderman, M.D., Ph.D., and Frederick Boerner, V.M.D. 4°, cloth, 845 pp., with 237 illustrations and 413 tables. Philadelphia: W. B. Saunders Company, 1949. $14.00.

It is erroneous in the practice of medicine to label a condition abnormal unless one knows what the wide range of normal is. For what is ambiguously called the average is merely the total value of all the items divided by the number of items. Therefore, the authors of this book have taken the term "norm" to represent the selected range of values that can be accepted as a standard, and they use the adjective "normal" for any measure that falls within the "norm." Then, with the aid of a large number of collaborators, each one of whom is an authority in a special field, they have accumulated a great deal of data of normal values encountered in the practice of clinical medicine. The book includes a chapter on the heart and one on electrocardiograms, and a section on the cellular elements, chemical components and physical elements of the blood, respiratory system and digestive system and so forth. It also has a section dealing with subjects in the specialists' fields, such as the skin appendages, eyes, ears, nose, throat, and it finally ends with a section of miscellaneous data — statistical data, food values, drugs and their doses, isotopes and life and actuarial tables.

The reviewer finds that this is an invaluable reference book for the clinician as well as the person who is doing research in medicine. Unless the wide range of normal values is known one is apt to regard as abnormal a condition that actually falls in the normal range.

The authors have even gone so far as to give an interpretation and normal range of values in various tests such as liver-function and renal-function tests.

Here is a valuable reference book that should be on the desk of every physician.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Doctors Courageous. By Edward H. Hume, M.D. 8°, cloth, 297 pp., with 23 illustrations. New York: Harper and Brothers, 1950. $3.50.

Dr. Hume, in this interesting book written in a narrative style, tells the story of the great Christian missionary doctors of Africa and Asia. The volume is well published and is recommended for all medical and public libraries.

Veterans Administration Technical Bulletins, Series 10. Vol. III, 1949. 4°, cloth, 159 pp. Washington, D. C.: United States Government Printing Office, 1950.

This volume comprises the manuscripts circulated among the staff of the Veterans Administration during 1949. The papers contain the most recent knowledge on the various subjects in the field of clinical medicine, and the series should be in large medical libraries for reference purposes.

Cancer Current Literature. Vol. I, No. 1, January, 1950. *An Index to Neoplastic Diseases.* 4°, paper, 55 pp. New York: American Cancer Society, 1950.

This new monthly list on cancer is a welcome addition to the bibliographies on special subjects that have been started during the past few years.

NOTICES

ANNOUNCEMENT

Dr. Louis Nathan announces the removal of his office to 475 Commonwealth Avenue, Boston.

BOSTON CITY HOSPITAL HOUSE OFFICERS' ASSOCIATION

The Boston City Hospital House Officers' Association will present a lecture as part of its evening lecture series in the Dowling Amphitheater of the Hospital on Tuesday, February 13, at 7 p.m. Dr. John Merrill, Peter Bent Brigham Hospital, will speak on the subject, "The Role of the Artificial Kidney in Fluid and Electrolyte Derangement." Discussers will be Drs. Arnold Relman, Massachusetts Memorial Hospitals, and Harold Levine, Peter Bent Brigham Hospital.

All interested persons are invited to attend.

MASSACHUSETTS TRUDEAU SOCIETY

A meeting of the Massachusetts Trudeau Society will be held in the auditorium of the Peter Bent Brigham Hospital on Tuesday, February 20, at 8 p.m. Dr. Donald S. King, consultant in tuberculosis, Veterans Administration, will speak on the subject, "Present Status of Antibiotic Therapy in the Treatment of Tuberculosis."

All interested persons are invited to attend.

NEW ENGLAND CARDIOVASCULAR SOCIETY

A meeting of the New England Cardiovascular Society will be presented by the staff of the Massachusetts Memorial Hospitals at the New England Mutual Hall, 225 Clarendon Street, Boston, on Monday, February 19, at 8 p.m., Dr. Robert W. Wilkins presiding.

PROGRAM

Roentgenologic Diagnosis of Pericardial Effusion. Drs. George Levene and Seymour A. Kaufman.

Selection of Cases for Limb Sympathectomy. Drs. Charles W. Robertson and Reginald H. Smithwick.

Cerebral Blood Flow during the Hypotensive Response to Intravenous Veriloid in Hypertensive Patients. Drs. Meyer H. Halperin, Franklin H. Epstein, Walter E. Judson, J. Donald Hatcher and Joseph R. Stanton.

The Effect of Graded External Pressure on the Vascular Volume of the Leg. Drs. Julius Litter and J. Edwin Wood.

The Effects of Elastic Stockings upon Thromboembolic Complications in Hospital Patients. Drs. George Mixter, Jr., Joseph R. Stanton, and Robert W. Wilkins.

Interested physicians and medical students are cordially invited to attend. (*Please note place of meeting.*)

AMERICAN CONGRESS OF PHYSICAL MEDICINE

The twenty-ninth annual scientific and clinical session of the American Congress of Physical Medicine will be held at the Shirley-Savoy Hotel, Denver, Colorado, from September 4 to 8. Scientific and clinical sessions will be given. All sessions will be open to physicians and other professional personnel. Full information may be obtained from the American Congress of Physical Medicine, 30 North Michigan Avenue, Chicago 2, Illinois.

SOCIETY MEETINGS AND CONFERENCES

FEBRUARY 9. Beta Iota Chapter of Nu Sigma Nu. Page 1018, issue of December 21.

FEBRUARY 9. Cutter Lecture. Page 116, issue of January 18.

FEBRUARY 11. National Conference on Medical Services. Page 38, issue of January 4.

FEBRUARY 12-14. American College of Allergists. Page 74, issue of January 11.

FEBRUARY 13. New England Society of Anesthesiologists. Page 512, issue of September 28.

FEBRUARY 13. Harvard Medical Society. Page 197, issue of February 1.

FEBRUARY 13. Springfield Academy of Medicine. Page 198, issue of February 1.

FEBRUARY 13. Boston City Hospital House Officers' Association. Page 237.

FEBRUARY 14. Beta Kappa Chapter of Nu Sigma Nu. Page 197, issue of February 1.

FEBRUARY 19. New England Cardiovascular Society. Notice above.

FEBRUARY 20. Massachusetts Trudeau Society. Notice above.

FEBRUARY 20. South End Medical Club. Page 198, issue of February 1.

FEBRUARY 21. Bay State Society for the Crippled and Handicapped. Page 1066, issue of December 28.

FEBRUARY 27. Norfolk District Medical Society. Page 629, issue of October 19.

MARCH 5-8. New Orleans Graduate Medical Assembly. Page 1018, issue of December 21.

MARCH 7. Hampshire District Medical Society. Page 170, issue of July 27.

MARCH 8. Some Fundamental Indications for the Use of Forceps. Dr. M. Fletcher Eades. Pentucket Association of Physicians. 8:30 p.m. Haverhill.

MARCH 11-16. College of Medical Evangelists. Page 74, issue of January 11.

MARCH 22. Hyman Morrison Lecture. Page 74, issue of January 11.

MARCH 26. Boston Lying-in Hospital Obstetric Round-Table Conference. Page 629, issue of October 19.

MARCH 27. Norfolk District Medical Society. Page 629, issue of October 19.

APRIL 9-13. American College of Physicians. Page 296, issue of June 15.

APRIL 10. New England Society of Anesthesiologists. Page 512, issue of September 28.

APRIL 24. Norfolk District Medical Society. Page 629, issue of October 19.

APRIL 28. American Psychosomatic Society. Page 198, issue of February 1.

MAY 8. New England Society of Anesthesiologists. Page 512, issue of September 28.

MAY 9. Norfolk District Medical Society. Page 629, issue of October 19.

MAY 16. New England Obstetrical and Gynecological Society. Hillcrest Country Club, Leicester, Massachusetts.

MAY 16-18. American Association of Genito-Urinary Surgeons. Page 160, issue of January 25.

MAY 22-24. Massachusetts Medical Society. Annual Meeting. Hotel Statler, Boston.

MAY 24-26. American Goiter Association. Columbus, Ohio.

SEPTEMBER 4-8. American Congress of Physical Medicine. Notice above.

SEPTEMBER 19. American Medical Writers' Association. Page 1066, issue of December 28.

SEPTEMBER 19-21. Mississippi Valley Medical Society. Page 1066, issue of December 28.

OCTOBER 31. New England Obstetrical and Gynecological Society. Hotel Somerset, Boston.

NOVEMBER 10-21. Pan-Pacific Surgical Association. Page 680, issue of October 26.

JULY 8-11, 1952. Thirteenth British Congress of Obstetrics and Gynaecology. Page xv, issue of December 14.

DISTRICT MEDICAL SOCIETIES

HAMPSHIRE

MARCH 7. 4:30 p.m. Cooley-Dickinson Hospital, Northampton.

MAY 2. 4:30 p.m. Annual Meeting. Jones Library, Amherst.

NORFOLK

FEBRUARY 27.

MARCH 27.

APRIL 24.

MAY 9. Annual Dinner.

All meetings except the Annual Dinner will be held at the Boston Medical Library, 8 Fenway, at 8:00 p.m.

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, FEBRUARY 15

THURSDAY, FEBRUARY 15

*9:00-10:00 a.m. Grand Rounds. Robert Breck Brigham Hospital.
*9:00-11:00 a.m. Medical Grand Rounds. Joseph H. Pratt Diagnostic Hospital.

FRIDAY, FEBRUARY 16

*9:00-10:00 a.m. Medical Conference. Joseph H. Pratt Diagnostic Hospital.
*9:00 a.m.-12:00 m. Combined Medical and Surgical Staff Rounds. Peter Bent Brigham Hospital.
*10:00 a.m. Surgical Clinic. South End Health Unit, 57 East Concord Street, Boston.
*12:00 m.-1:00 p.m. Pediatric Clinicopathological Conference. Joseph H. Pratt Diagnostic Hospital.
*1:30 p.m. Tumor Clinic. Out-Patient Department, Mount Auburn Hospital, Cambridge.

SATURDAY, FEBRUARY 17

*9:00-10:00 a.m. Surgical Grand Rounds. Joseph H. Pratt Diagnostic Hospital.

MONDAY, FEBRUARY 19

*11:30 a.m.-12:15 p.m. Clinical Conference. South End Health Unit, 57 East Concord Street, Boston. Dr. Cleaveland Floyd in charge.
*12:15-1:15 p.m. Clinicopathological Conference. Main Amphitheater, Peter Bent Brigham Hospital.
*8:00 p.m. New England Cardiovascular Society. New England Mutual Hall.

TUESDAY, FEBRUARY 20

*9:00-10:00 a.m. Medical Conference. Joseph H. Pratt Diagnostic Hospital.
*12:15-1:15 p.m. Clinicoroentgenological Conference. Peter Bent Brigham Hospital.
*1:30-2:30 p.m. Pediatric Rounds. Burnham Memorial Hospital for Children. Massachusetts General Hospital.
*8:00 p.m. Massachusetts Trudeau Society. Auditorium, Peter Bent Brigham Hospital.

WEDNESDAY, FEBRUARY 21

*11:00 a.m.-12:00 m. Medical Clinic, including Psychiatric Conferences. (Children's Medical Center.) Amphitheater, Children's Hospital.
*12:00 m. Medical Discussion. Margaret Jewett Hall, Mount Auburn Hospital, Cambridge.
*12:00 m.-1:00 p.m. Clinicopathological Conference. (Children's Medical Center.) Amphitheater, Peter Bent Brigham Hospital.
*2:00-3:00 p.m. Combined Clinic of all services. (Children's Medical Center.) Amphitheater, Children's Hospital.

*Open to the medical profession.